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ACTA RADIOLOGICA

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ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE ET SUECIAE

VOL. 41 FEBRUARY 1954 FASC. 2

ROENTGENOLOGIC STUDIES OF THE INTESTINE IN NORMAL INFANTS AND IN COLONIC HYPERPERISTALSIS IN NEUROLABILE INFANTS

by

Sigvard Jorup and *Sven Roland Kjellberg*

It is characteristic of so-called dyspepsia in breast-fed infants for defaecation to occur during each feeding, occasionally after or between feedings. The stools are often expelled with force; they are loose and watery, usually green, contain mucus and have a normal, acid smell. The infants are restless, they whine and are irritable, particularly during feeding, when they often have attacks of abdominal pain and therefore stop sucking. The pain is usually intermittent and ceases at the end of feeding but may persist for some time. Some mothers complain that their infants suffer from flatulence and meteorism. The frequent motions lead to intertrigo on the buttocks. These lesions nevertheless respond rapidly to treatment and are evidently secondary to the loose stools. The infants do not appear to suffer from allergy to any marked extent, at any rate as manifested by signs on the skin or in the respiratory tract. A slight exudative diathesis is occasionally found. The condition usually starts during the first week of life and seldom persists after the third or fourth month. It is not unusual for it to disappear earlier.

The great majority of the infants are neurolabile. A striking fact is that in the majority of cases the mother, and not infrequently the father as well, are nervous and neurolabile. In most cases one or both parents — usually the mother — have gastro-intestinal disturbances such as diarrhoea, pain, a feeling of discomfort or vomiting when nervous or irritable.

The general condition of such infants is relatively good and the gain in weight is usually fairly satisfactory. Because they are restless and

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From the Children's Hospital 'Samariten', Stockholm, Sweden.

cry excessively, they are often a source of irritation in the home, especially at night.

The opinions in the literature are extremely divergent with regard to the cause of so-called dyspepsia in breast-fed infants. Many authors have expressed the view that it is due to overfeeding, to underfeeding, or to frequent and irregular feedings. These cannot, however, be the only causes since a change in the amount of food or regularization of the meals fails to lessen the frequency of defaecation. Other authors have attributed the dyspepsia to the breast-milk itself, to variations in its composition, *e. g.* in the fat content. It has, however, been demonstrated that a wet-nurse can feed a normal infant and a dyspeptic infant at the same time, with no change either in the frequency of the stools or in their appearance in either infant. WEILL spoke of allergy and anaphylaxis to human milk; he tried subcutaneous injections of human milk to produce desensitization, in most cases unsuccessfully. The theory of increased fermentation in the intestine, leading to increased peristalsis, has many adherents. On the basis of this theory, RACZYNSKI recommended giving 100 grams of cow's milk twice daily. Other authors have advised protein preparations such as Larosan or Laktén. It has not been possible to discover any bacteriologic cause for this symptom complex. Infectious conditions are not infrequently accompanied by diarrhoea, but they differ from dyspepsia in breast-fed infants not only with respect to the rise in temperature and loss of weight, but also with regard to the history.

Case Material

The case material consisted of:

A. 38 children from 1 week to 4 months of age from the Samariten Children's Hospital and the Child Welfare Centres of the City of Stockholm, who exhibited no signs or symptoms of disease on medical examination.

B. 111 children of both sexes, from 2 weeks to 11 months of age, suffering from dyspepsia in breast-fed infants.

Technique

For the roentgenologic studies, barium contrast medium was given both by mouth and as an enema. A special catheter (Ameran acmi 20, inflate 20 cc) was used for the *contrast enema*. It was injected at a pressure of 50 cm of water. When severe dyspepsia was present it was, however, necessary to increase the pressure to 80 cm of water or above. When the colon was well filled with the contrast medium, the catheter was removed and the infant allowed to evacuate the enema during the subsequent five minutes. If at the end of this time the infant continued

to evacuate the enema, or fluoroscopic screening showed that motility was still in progress in the colon, the period was extended. When defaecation had been completed, the mother lay down on the trochoscope and the infant was put to the breast. The appearance of the colon and its movements were then studied during the feeding.

For a study of the *transit through the intestine*, 5 teaspoonfuls of barium contrast medium (Pharmabaryt) were given mixed in water, breast-milk or cow's milk mixture. As soon as the barium had filled the duodenum, the infant was put to the breast. The appearance of peristalsis and the transit of the contrast medium were studied before, during and after feeding. Continuous examinations were subsequently made at intervals of one to two hours, a feeding being given on each occasion. In some cases, however, no food was given until some of the contrast medium had reached the colon.

In order to study the effect of different factors in the intake of food, we made examinations during:

1) ordinary breast-feeding;
2) sucking at a nipple shield and an unperforated or perforated teat, respectively, without the presence of the mother;
3) sucking at an empty breast;
4) sucking from a cleansed nipple;
5) bottle-feeding (breast-milk, citric acid milk and cow's milk mixture);
6) tube feeding;
7) spoon feeding;
8) fondling the child without feeding.

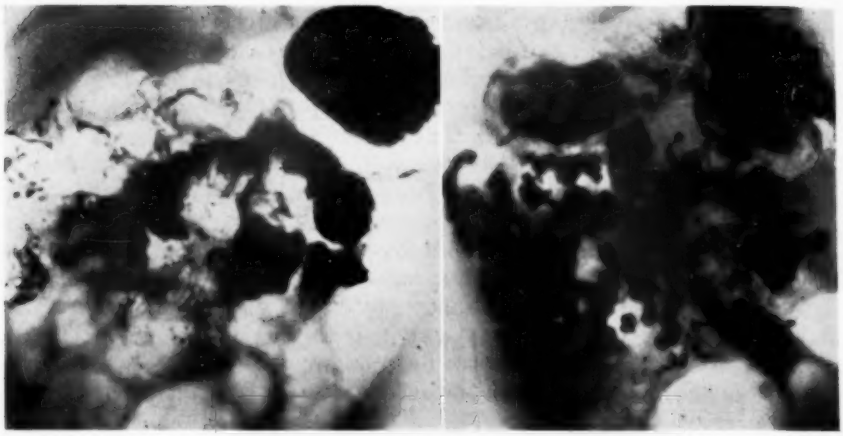
Results

1. *Stomach*

No difference between the normal and the dyspeptic infants could be observed with respect to the appearance of peristalsis or emptying of the stomach. The amount of gas present in the stomach was approximately the same in both categories.

2. *Small intestine*

Approximately 12 to 15 seconds after the infant had been put to the breast (or given food in some other way) vigorous motility started in the duodenum and propelled the barium rapidly onwards. This movement spread quickly to the other parts of the small intestine (Fig. 1 a—c) and after 35 to 45 seconds could be observed in its middle third. It usually reached the terminal ileum after from 80 to 105 seconds. In the jejunum, the contrast medium was divided up into small portions the size of a pea or bean, which were propelled onwards with great rapidity. On the fluorescent screen they resembled small animals darting hither and thither in the abdominal field.



a. b.

c.

Fig. 1. Normal transit through the intestine.

a. 23 mins. after barium meal.

b. 25 mins. after barium meal, 2 mins. after beginning of breast-feeding.

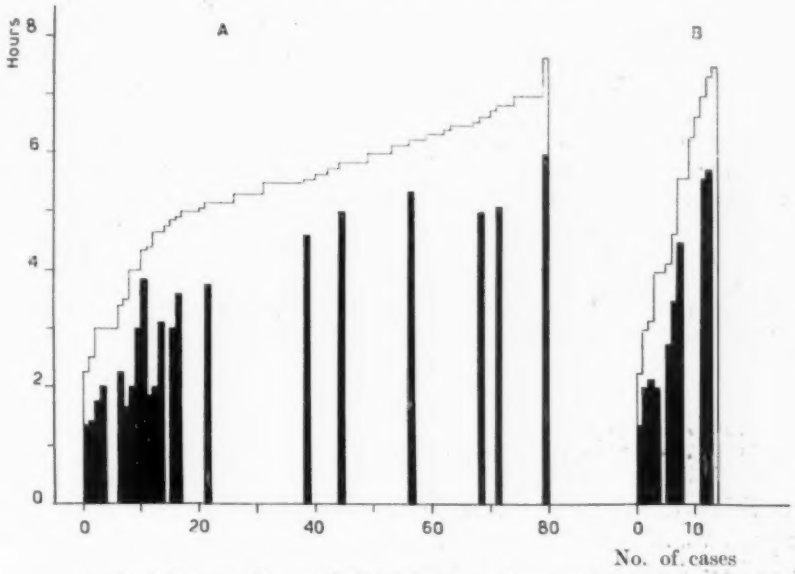
c. 33 mins. after barium meal; breast-feeding completed.

When the barium gradually reached the ileum, a change took place in the appearance of peristalsis. The barium was assembled in larger portions, the contractions became more kneading and the rate of transit slower. This was particularly apparent in the terminal ileum. When, approximately $1\,^1/_2$ minutes after the beginning of feeding, motility had reached the terminal ileum, this part of the intestine started to contract and parts of the contrast medium were forced into the caecum.

The aforementioned conditions were observed during the actual

Table 1

Rate of transit through the small intestine.

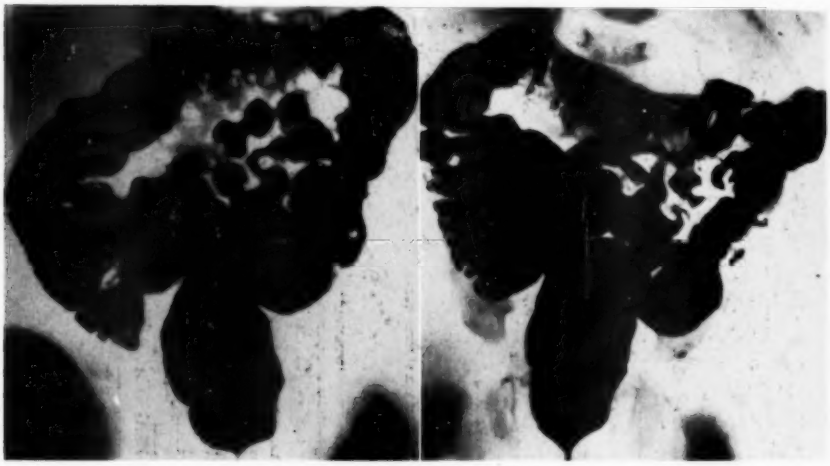


A. In infants with so-called dyspepsia of breast-fed infants.
B. In normal infants.

The upper indented lines denote the time at which the barium was definitely present in the colon. The black columns denote the time at which the last examinations were made; the barium was then present in the small intestine only.

feeding (or the administration of food other than breast-milk). Towards the end of feeding and especially when it had ceased, the motility decreased, particularly in the jejunum. When the infant was examined between two feedings, fairly slow motility was seen, not only in the ileum but also in the jejunum; the separation of the barium into small portions was considerably less marked. No difference between the healthy and the dyspeptic children could be noted as far as the general picture was concerned, nor were any differences found with the various methods of feeding.

It has been stated by CATHALA, among others, that the symptom complex is caused by increased fermentation resulting in more rapid peristalsis and transit. A closer analysis was therefore made of the rate of transit in both normal and dyspeptic infants. The results are recorded in Table 1. No difference was observed in the rate of transit in the healthy and the dyspeptic infants, respectively. As may be inferred



a. Before breast-feeding. b. After breast-feeding.

Fig. 2. Normal infant. Contrast enema.

from Table 1, the rate of transit ranged, in round figures, from 2 to 7 hours in both categories of infants. This is in good agreement with the investigations made by LÖNNERBLAD on children about one year of age.

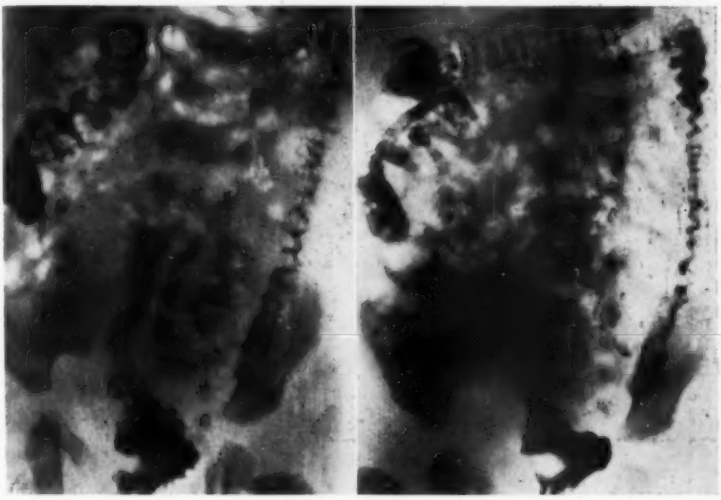
3. *Colon*

1) *Colon enema*

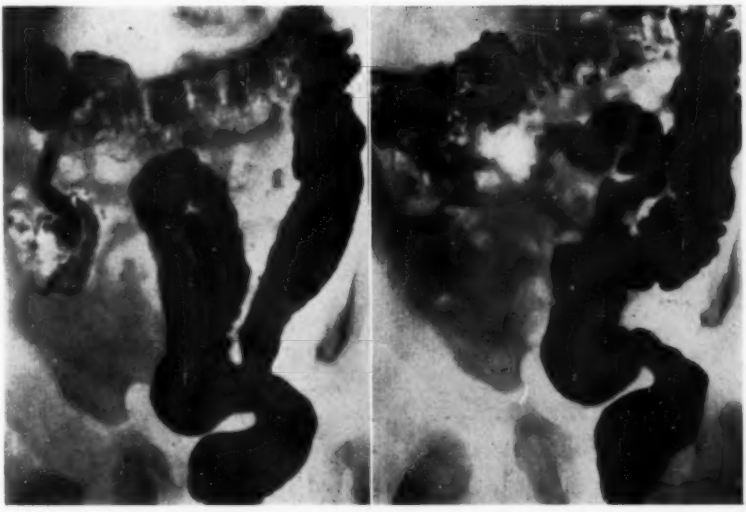
A. *Normal infants.* In these infants it was extremely easy to inject the enema at a pressure of approximately 50 cm of water. The colon dilated to a considerable width and after defaecation fairly large quantities of barium remained in the relatively distended colon. During breast-feeding (or feeding by other means) little, or only inappreciable, motility was visible in the colon. The movement only altered the shape of the colon and no marked propulsion of the barium could be observed (Fig. 2).

In two of the normal infants, the change in the shape of the colon was fairly pronounced during the feeding and some propulsion of the barium took place. This was accompanied by slight defaecation which was, however, slow and not of the explosive nature often seen in children with hyperperistalsis.

B. *In so-called dyspepsia in breast-fed infants.* Injection of the enema frequently involved considerable difficulties in these infants. In severe cases, the colon contracted violently and a pressure of 80 cm of water or more was necessary for filling of the colon. Owing to the increased

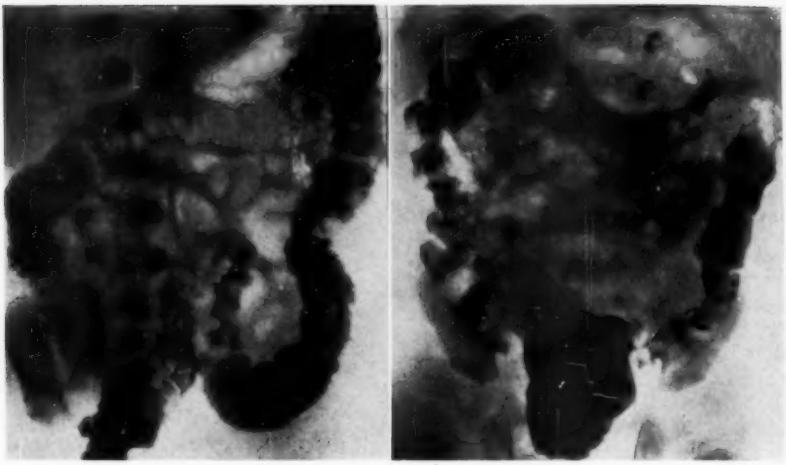


a. Before breast-feeding. b. After breast-feeding.

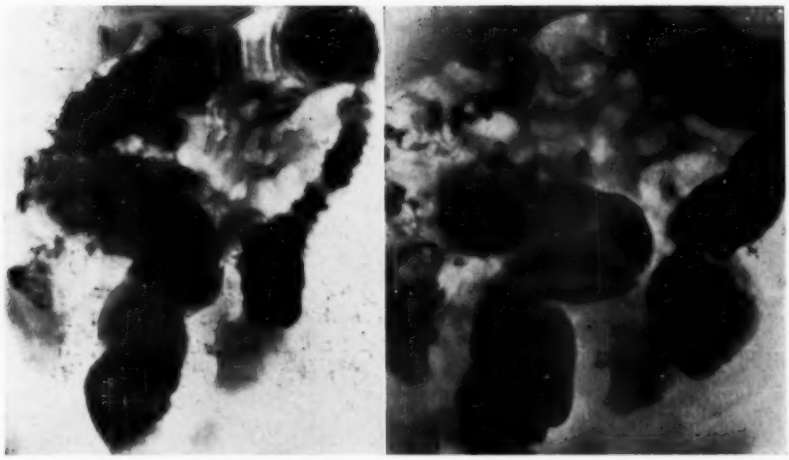


c. Before breast-feeding. d. After breast-feeding.

Fig. 3. Severe hyperperistalsis. Contrast enema. a. and b. Before Skopyl therapy. c. and d. After Skopyl therapy.



a. Before breast-feeding. b. After breast-feeding.



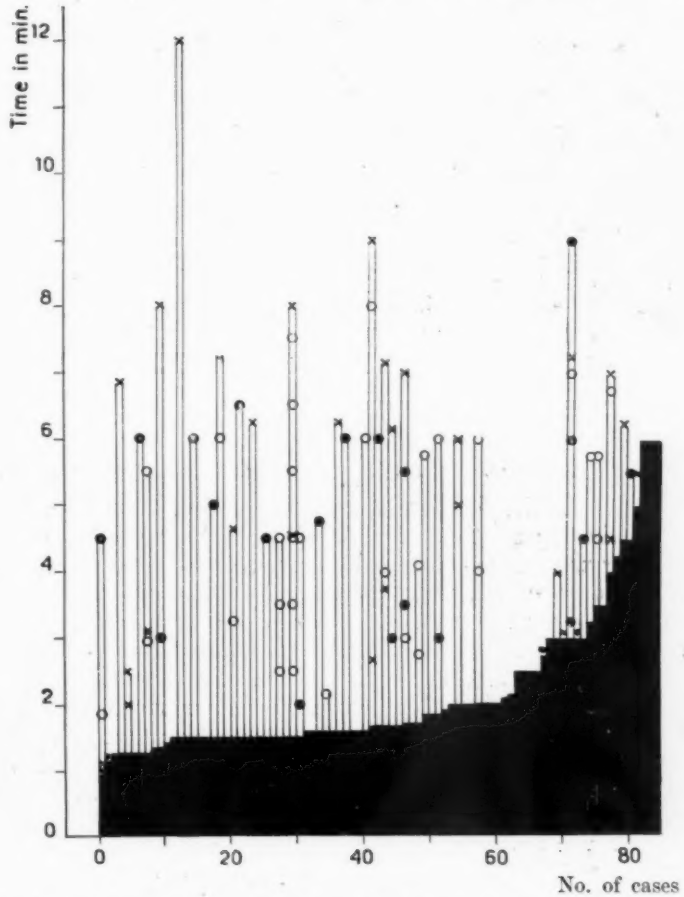
c. Before breast-feeding. d. After breast-feeding.

Fig. 4. Slight hyperperistalsis. Contrast enema. a. and b. Before Skopyl therapy. c. and d. After Skopyl therapy.

tendency to contraction in the colon, a shower of barium was often evacuated from the anus when the catheter was removed. In some of the infants, it was projected to a distance of about one metre. In severe cases, the entire colon contracted violently and practically all the barium

Table 2

Colonic peristalsis, attacks of pain, and defaecation.



The dark areas denote the onset of a wave of peristalsis in the colon after the beginning of feeding.

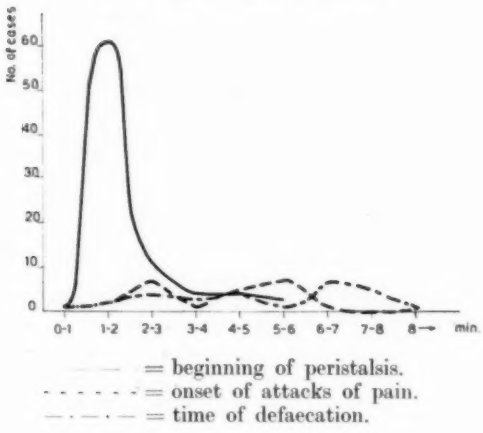
× = time at which defaecation occurred after feeding.

○ = time of onset of attacks of pain after beginning of feeding.

was expelled in a short time (Fig. 3). In less severe cases, a varying amount of contrast medium remained in the colon (Fig. 4). When a dyspeptic infant was put to the breast (or fed by other means) a vigorous contraction was visible in the caecum about 1 1/2 minutes after feeding

Table 3

Frequency curve of Table 2.



started. This propelled the contents onwards and the peristaltic waves were rapidly transmitted to the other segments of the colon. The more marked the dyspepsia, the more rapid was the motility. It was not uncommon for the entire colon to be emptied within 30 seconds. In less severe cases, the barium was propelled by this first peristaltic wave only as far as the transverse or descending colon, where it remained until a new wave of peristalsis started, usually after about 4 to 6 minutes. This latter wave propelled the barium further and a varying amount was evacuated (Tables 2 and 3). When these contractions occurred, particularly when they reached the sigmoid, the child became restless, ceased sucking and sometimes screamed. When the wave of peristalsis ceased, the child became calm, took the nipple and started to suck as before.

2) *Transit through the intestine*

In order to ensure that the increased peristalsis in the colon was not caused by the enema, an additional study of the transit through the colon was made in the majority of cases. When the barium had reached the colon and partly filled it, the child was — as stated earlier — put to the breast (or fed by other means). As also mentioned previously, about 1 $^1/_2$ minutes after the beginning of feeding, peristalsis started in the terminal ileum and the barium was ejected into the caecum. This was accompanied, about 100 seconds after the beginning of feeding, by contractions of the caecum, which spread rapidly to the other segments of the colon. No essential difference could be noted with the respective

forms of examination (Figs. 3 a—b and 7 c—d). In mild cases of dyspepsia the contractions of the colon were, however, possibly slightly stronger when a barium enema was given than after a barium meal.

3) *Sucking experiments*

It has long been known that the aforementioned type of dyspepsia occurs mainly in breast-fed infants. For this reason other food has been given as a supplement to breast-milk. In some cases the infants have even been weaned in order to eliminate the factor that was considered to be the only, or the main, cause of the disorder, *i. e.*, the nature of the food.

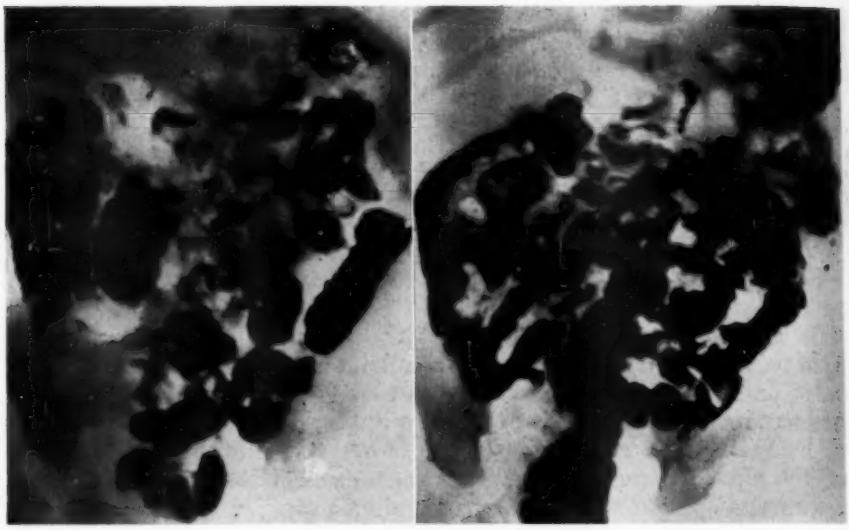
It is a long-established fact that the ingestion of food produces a peristalsic movement in both the small intestine and the colon. MACEVEN, and later HERTZ, demonstrated that food present in the stomach produces intestinal peristalsis; the latter author denoted this phenomenon as the gastro-colic reflex. HOLZKNECHT observed motility in the colon shortly after the ingestion of a contrast meal. WELCH and PLANT expressed the opinion that the term "feeding reflex" was more adequate. This was because they found that the ingestion of food produced activity in the colon in the dog and in man, whereas they were unable to produce this movement when food was given through a gastrostomy opening. CANNON found a close relationship between the intake of food and defaecation and considered that it was not possible to distinguish between the gastro-colic reflex and the feeding reflex. IVY found that, at any rate in the dog, the gastro-colic reflex is a duodeno-colonic reflex since stimulation of the duodenum and the upper part of the jejunum resulted in defaecation, whereas distension of the stomach had no such result.

GALLAPEAUX and TEMPLETON gave buttermilk by stomach tube and noted increased colonic motility within 50 minutes. Their experiments were made in animals. They also found that in 'untrained animals' distension of the stomach by means of a balloon was as effective in causing defaecation as filling of the stomach with yeast or buttermilk. RODRIGUEZ expressed the opinion that the frequent defaecations in so-called dyspepsia in breast-fed infants may be due to a gastro-colic reflex.

Since we considered it important from a therapeutic point of view to ascertain the influence of the respective factors in the intake of food on colonic motility, we made a study of each of them separately.

(1) Sucking at an empty breast

In five cases in which the mother had no milk, the infant was put to the breast in the usual way. In two of these cases, some difficulty was



a. Before sucking. b. After sucking.

Fig. 5. Hyperperistalsis. Sucking at an empty breast.

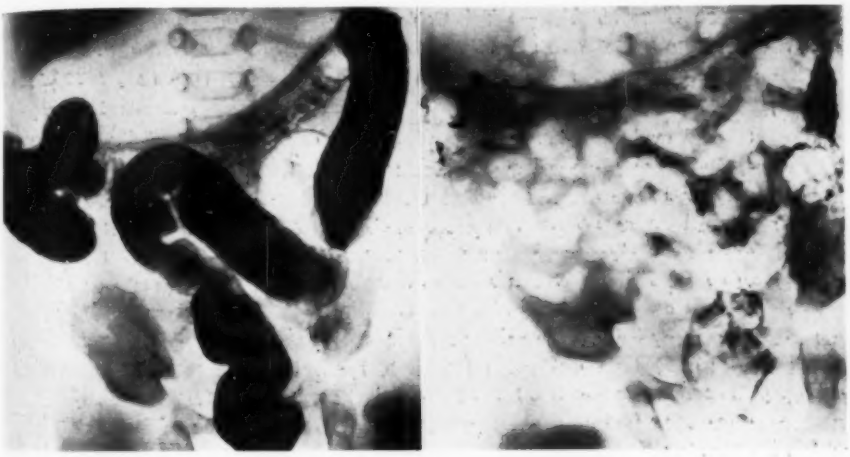
experienced in getting the child to take the breast. The same technique as that described previously, *i. e.*, a barium enema and a barium meal, was used for the examination. In three of the dyspeptic infants, sucking at the empty breast produced strong colonic peristalsis; in two of these cases it terminated in defaecation (Fig. 5). The experiment was repeated on one child after thorough cleansing of the breast with alcohol and ether. During the subsequent "feeding" no peristalsis was visible in the colon.

(2) Sucking from a cleansed breast

In three cases, the breast of the nursing mother was cleansed with alcohol and ether; these were allowed to evaporate and the child put to the breast in the usual way. In the dyspeptic children, the feeding resulted in strong waves of peristalsis in the colon, ending in defaecation (Fig. 6). Peristalsis was possibly slightly less vigorous than when the breast had not been cleansed.

(3) Sucking at an unperforated teat

a. An unperforated teat, moistened with breast-milk or citric acid milk, was attached to a nipple shield and applied to the mother's breast. In one dyspeptic infant, vigorous propulsive peristalsis was observed



a. Before sucking. b. After sucking.

Fig. 6. Hyperperistalsis. Sucking from a cleansed breast.

in the colon, as well as an attack of pain two minutes after sucking commenced; in another case there was a slight propulsive movement while in a third, non-propulsive motility was noted in the colon. No colonic motility could be observed in the other five dyspeptic infants; this also applied to one normal infant.

b. The infants were allowed to suck at a teat moistened with a drop of water and attached to an empty bottle. The mother was not present during the experiment. In one case of severe dyspepsia — the same infant who exhibited vigorous propulsive peristalsis in the colon during experiment *a* — slight propulsive peristaltic activity was observed in the colon, accompanied by slight pain. In two cases slight contracting, non-propulsive motility was visible in the colon. In a further three children, one of whom was normal, no colonic motility could be discerned.

c. The transit through the small intestine was studied during experiments *a* and *b* on 8 occasions (6 children). In every instance the appearance of motility was normal. The peristaltic waves reached the terminal ileum approximately one minute after the child started to suck.

(4) Fondling the child

In a considerable number of cases, the mother lay on the trochoscope and fondled her child. Intimate contact was thus established, but the child was not allowed to take the breast. No peristalsis or defaecation was produced by this means.

Table 4

Results of Treatment.

	Effect			
Skopyl	Prompt	Good	Moderate	None or poor
Clinical evaluation	40	14	7	—
Roentgen examination	36	4	3	2
Laktén or Larosan				
Clinical evaluation	—	—	2	9
Roentgen examination	—	—	—	10
Cow's Milk Mixture or Citric Acid Milk				
Clinical evaluation	—	—	—	20
Roentgen examination	—	—	—	14
Change of Environment				
Clinical evaluation	—	—	3	23
Roentgen examination	—	1	—	13
No Treatment				
Clinical evaluation	—	—	3	17
Roentgen examination	—	2	1	12

(5) Feeding with a teat and bottle

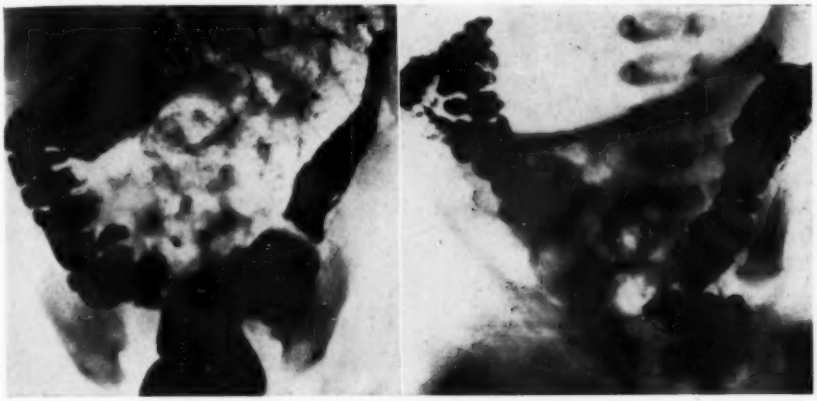
In 16 cases the infants were fed with a teat and bottle; the mother was not present. The bottle contained breast-milk, citric acid milk or cow's milk mixture. Two of the children were normal children; neither colonic motility nor defaecation resulted. In 8 of the remaining cases there was lively peristaltic activity in the colon, terminated by defaecation in 5 cases (Fig. 7). In one case copious motions were passed but no peristalsis could be observed either in the caecum or in the transverse colon. There was no difference in the appearance of the movements when breast-milk and cow's milk mixtures, respectively, were given.

(6) Tube feeding

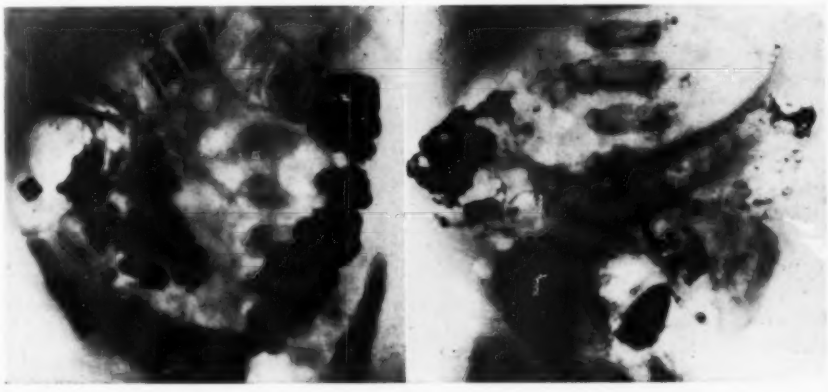
In an attempt to eliminate the sucking factor, the feeding was given by tube in 11 cases (2 normal children). Three of the children with so-called dyspepsia exhibited moderate colonic motility; two of them defaecated (Fig. 8). No peristalsis in the colon was observed in the normal children.

(7) Spoon feeding

Moderate colonic peristalsis with defaecation was observed in 5 of the children with dyspepsia, and slight to moderate peristalsis in 2 (Fig. 9). One of the three normal children displayed extremely slight colonic motility without propulsion, but in no case did defaecation occur.



a. Before feeding. b. After feeding.



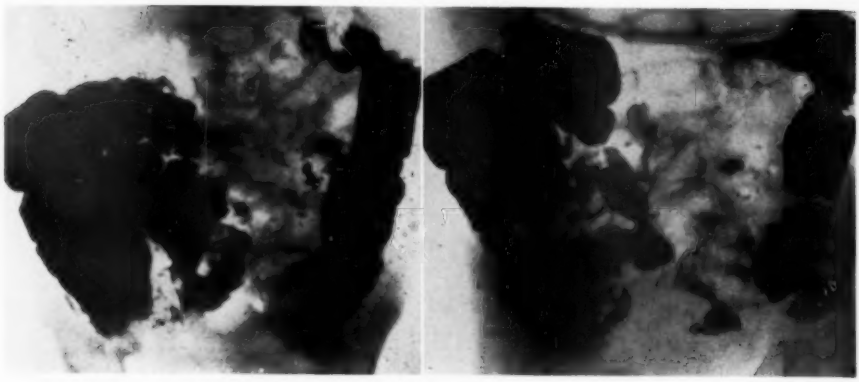
c. Before breast-feeding. d. After breast-feeding.

Fig. 7. Hyperperistalsis. Feeding with a teat and bottle.

A graphic survey of the results of the sucking experiments is given in Table 5.

Pressure Measurements

In order to obtain information regarding pressure and its variations in the colon of both normal infants and those suffering from so-called dyspepsia in breast-fed infants, pressure measurements in the rectum were made in 16 cases. A heart catheter connected to a Tybjærg-Hansen Universal Manometer was used for this purpose.



a. b.

c.

Fig. 8. Hyperperistalsis. Tube feeding.

a. Before feeding.

b. After feeding.

c. After breast-feeding.

In the normal infants, the pressure in the rectum during feeding was up to 60 cm of water; the variations were small, not exceeding 25 cm of water, and did not take place abruptly. Children who had earlier suffered from dyspepsia and had become normal differed from the essentially normal children in that the variations in pressure were greater. The infants with severe dyspepsia exhibited, during breast-feeding or other feeding, remarkably high pressure — the majority with a maximum exceeding 100 cm of water — as well as considerable variations in pressure. One infant had a variation in pressure of over 100 cm. In three cases of severe dyspepsia, the infants were re-examined after Skopyl therapy; the values were then lower and the variations less marked (Table 6 and Diagram 1).

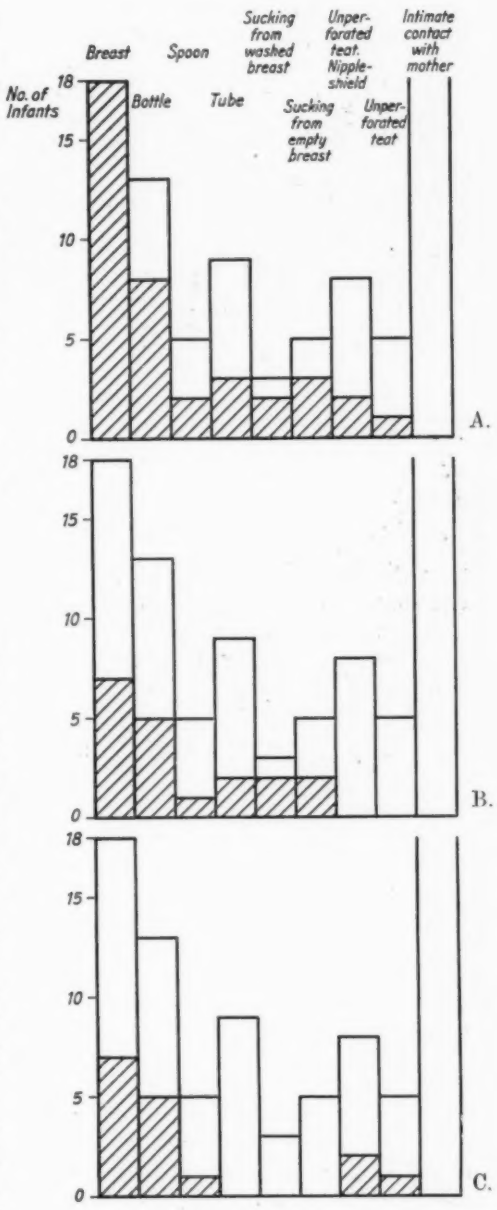
Table 5

Experiments in feeding by different methods including the elimination of various factors in the reception of food, and the influence on colonic peristalsis defæcation and attacks of pain.

A. Propulsive colon motility. Shaded columns signify propulsive colon motility; unshaded columns no or insignificant propulsive colon motility.

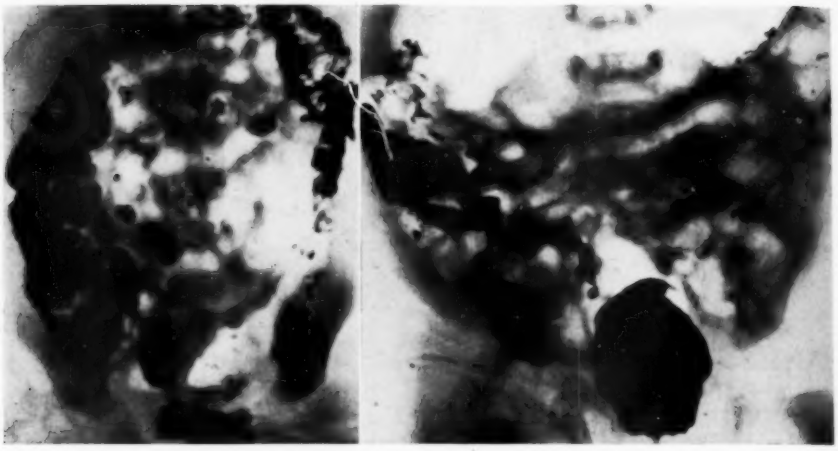
B. Defæcation. Shaded columns signify defæcation during roentgen examination; unshaded columns no defæcation.

C. Attacks of pain. Shaded columns signify attacks of pain during roentgen examination; unshaded columns no attacks.



Therapy

Reports have been given in the literature of good results in the treatment of so-called dyspepsia in breast-fed infants with atropine (JUNDELL, MARFAN, RODRIGUEZ). We therefore started to give Skopyl (0.05 mg of methyl scopolamine per drop) to such infants at the Samariten Children's Hospital. The drops were administered 20 to 30 minutes before each feeding. During the first three days one drop was given; if this failed to bring about the desired results the dose was increased to 2 and later, in some cases, to 3 drops. With the last-mentioned dose, signs of overdosage were, however, observed in one case. As may be inferred



a. Before feeding. b. After feeding.

Fig. 9. Hyperperistalsis. Spoon feeding.

from Table 4, the results of treatment were satisfactory. Even the smallest dose sufficed in the majority of cases to make the stools normal almost at once. The attacks of pain ceased or became less severe and the infants, who had previously been restless, became quiet and were no longer disturbing at night.

Roentgenologic Examination after Treatment

A. *Skopyl*

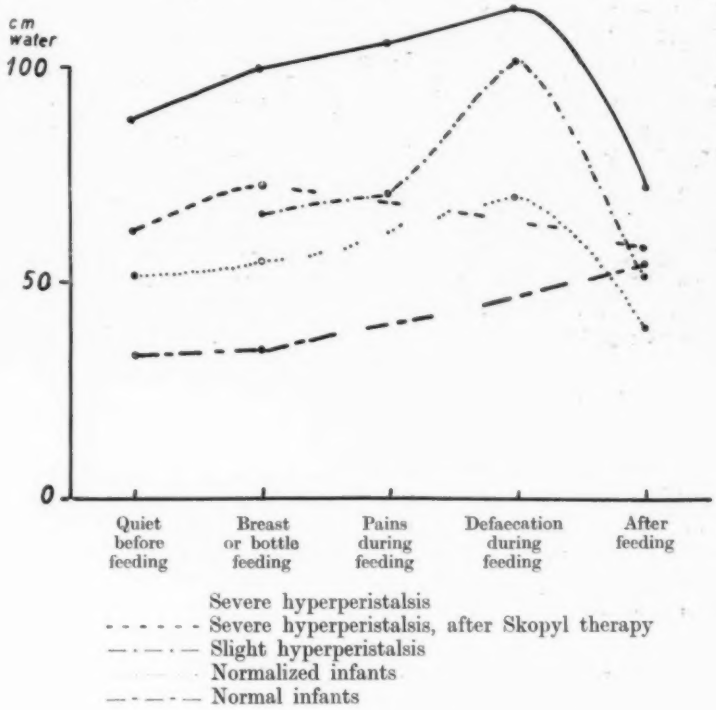
The results of treatment were also apparent roentgenologically. When the effect was satisfactory, roentgenologic examination showed a colon of normal width, which was easily filled by the contrast medium (Fig. 10 c—d). During feeding, no peristalsis was visible but possibly a slight change in the shape of the colon. If, on the contrary, the therapeutic results were unsatisfactory, there were still signs of hyperperistalsis in the colon. As the condition became normal, these signs gradually disappeared.

B. *Protein preparations or cow's milk*

Raczynski recommended a supplement of 100 grams of boiled cow's milk twice daily, and Czerny and Keller "allaitement mixte". At the Child Welfare Centres in Stockholm, a supplement of boiled cow's milk to every feed is often prescribed. This has not, however, resulted in

Table 6

Mean of highest rectal pressures measured.



any great improvement. In a few cases the stools became somewhat firmer but the frequent defaecations and attacks of pain persisted.

In the present series, 30 dyspeptic infants were given Larosan, Laktén (calcium caseinate) or various mixtures of cow's milk. This treatment brought about no change in the condition, neither clinically nor roentgenologically (Fig. 10 a—b).

C. *Untreated, and treated by change of environment, respectively*

In addition to these treated groups, 46 infants were kept under observation for varying periods. This was in order to study the return to normal which takes place sooner or later in such cases. Follow-up roentgenological examinations were made on 29 of these patients. The rapidity with which the return to normal occurs depends on the age

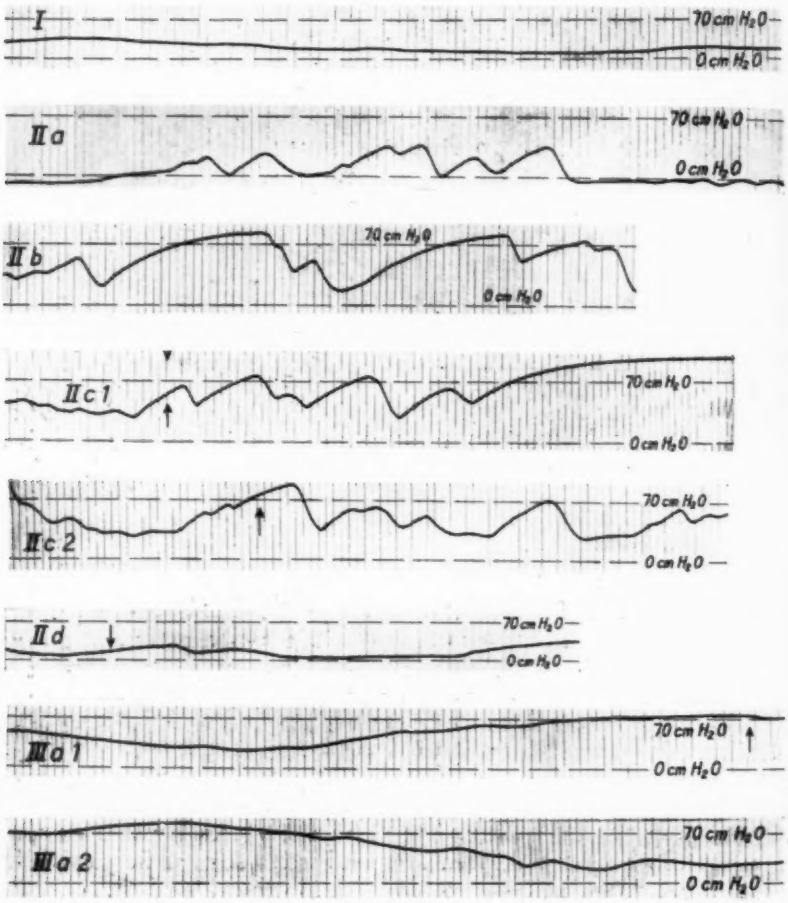


Diagram 1. Pressure measurements in the rectum.

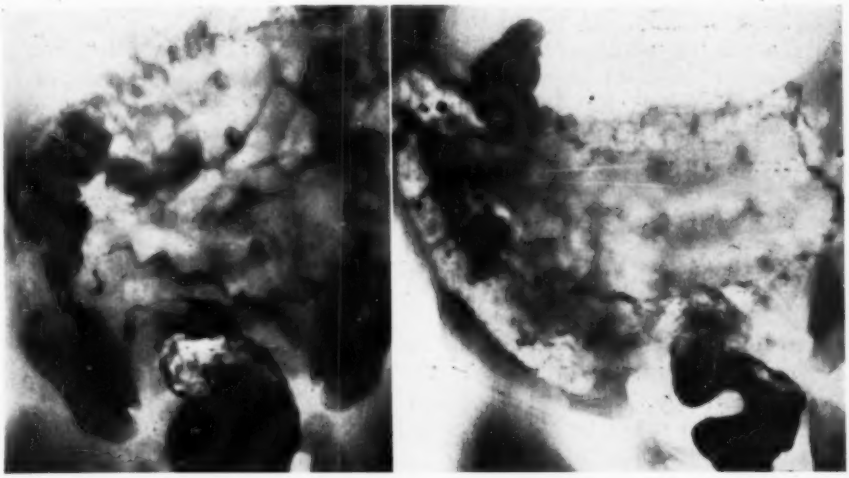
No. I. Normal case. During feeding.

No. II. Case of severe dyspepsia.

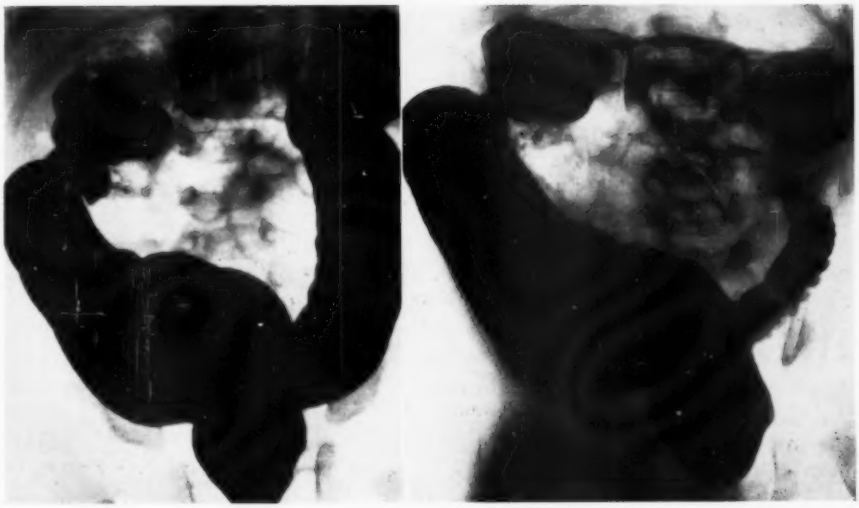
a. During breast-feeding. b. After breast-feeding. c 1 and c 2. Breast-feeding. Defaecation. Commencement indicated by arrow. d. Following Skopyl. Normal. Breast-feeding. Arrow indicates time when slight defaecation occurred.

No. III. Case of severe dyspepsia.

a 1. Breast-feeding. The arrow indicates defaecation. — a 2. Continuation of the curve. Breast-feeding continues.



a. Before breast-feeding. b. After breast-feeding.



c. Before breast-feeding. d. After breast-feeding.

Fig. 10. Hyperperistalsis.

a. and b. After Laktén therapy. c. and d. After Skopyl therapy.

of the child and the severity of the disorder; the latter may be evaluated roentgenologically. We found that the rate of the return to normal was unaffected by whether or not the infants were given supplements of protein preparations or cow's milk mixtures. In the case of children admitted as in-patients to the Samariten Children's Hospital, the change of environment had a favourable effect, especially on the neurolabile symptoms and the constant screaming. The effect on the attacks of pain was slighter and the effect on the frequency and appearance of the stools was still less.

Discussion

Judging by the results of our investigations, the symptoms in so-called dyspepsia in breast-fed infants are wholly to be attributed to the colon. An interesting fact is that in these cases, peristalsis starts in the colon approximately at the same time as the activity in the small intestine reaches the terminal ileum. A plausible explanation is that the possible stimulation exerted by the terminal ileum on the colon is blocked in normal cases at the level of the ileocaecal valve, whereas this blocking does not take place in hyperperistalsis. The good effect of Skopyl lends some support to this hypothesis.

The investigation also showed that the appearance of motility in the small intestine was the same in normal children as in those with dyspepsia. Nor could any difference be observed in the rate of transit in the respective categories.

The mechanism initiating intestinal peristalsis appears on the basis of our investigations to have several components, each of which is independently capable of producing peristalsis. In our opinion, the best therapy in cases of so-called dyspepsia in breast-fed infants is the administration of a drug decreasing the excitability of the autonomic nervous system. The current method of treating such children by changing the composition of their food appears to be of little or no value.

Clinical studies have shown that dyspeptic infants, practically without exception, exhibit neurolabile symptoms. Their relations are also to a great extent neurolabile and show a higher incidence of 'nervous' gastro-intestinal symptoms than the relations of normal infants. In our opinion, the most adequate name for this syndrome is 'colonic hyperperistalsis in neurolabile infants'.

SUMMARY

A description is given of roentgenologic observations in colonic hyperperistalsis in neurolabile infants. The colon of such infants is found to exhibit increased irritability whereas the stomach and small intestine present a normal picture. The condition is considerably improved by the administration of methyl scopolamine.

ZUSAMMENFASSUNG

Röntgenologische Beobachtungen über Dickdarmhyperperistaltik bei neurolabilen Säuglingen werden geschildert. Der Dickdarm derartiger Säuglinge zeigte eine gesteigerte Reizbarkeit; Ventrikel und Dünndarm hingegen wiesen ein normales Bild auf. Der Zustand wird durch Zufuhr von Methyl-Skopolamin erheblich verbessert.

RÉSUMÉ

Les auteurs décrivent des signes radiologiques de l'hyperpéristaltisme du colon chez les nourrissons neurolabiles. Le colon de ces nourrissons présente une irritabilité augmentée alors que l'estomac et l'intestin grêle donnent une image normale.

Cette affection est considérablement améliorée par l'administration de méthyl-scopolamine.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: Sv. A. CHROM), THE CENTRAL HOSPITAL, HILLERØD, DENMARK

ROENTGEN EXAMINATION IN ACUTE OR CHRONIC APPENDICITIS

by

Sv. A. Chrom and *C. E. Gudbjerg*

It is a well-known fact that the clinical diagnosis of acute or chronic appendicitis may be attended with great difficulties, and that none of the many methods of clinical examination devised for that purpose are absolutely reliable and satisfactory.

However, as early as 1909, when BÉCLÈRE published a report on a patient in whom he had visualized a bismuth-filled appendix in a roentgenogram three years previously, it was hoped that roentgenography would ultimately provide a valuable and more reliable diagnostic aid in these conditions. A large number of reports on roentgen examination in chronic appendicitis have appeared, particularly during the inter-war period. Space does not permit an extensive historical review of these reports but, in recapitulation, it may be said that roentgen examination in appendicitis proved disappointing, and many investigators claimed that it was of no value at all. This view was held by VILLUM JENSEN (1939), who is so far the only Danish writer to have published a paper on the subject.

In discussing the pathology of appendicitis with a reasonable amount of certainty it is necessary to have a series of normal controls (the reader is referred to our paper, "Studies on Contrast Filling of the Normal Appendix", of which the present paper is a continuation).

Nothing definite can be said as to the etiology and pathogenesis of acute appendicitis. BOYD draws a distinction between exciting factors and predisposing causes and, among the former, mentions infection and obstruction. Formerly, it was generally believed that infection was the more dominant of these factors, and that the bacteria responsible for the inflammation invaded the appendix directly from the cecum or, in exceptional cases, from the blood stream, for example in association with

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acute tonsillitis. Now, however, it seems as if obstruction is a more important initial exciting factor.

It can scarcely be doubted that there is an intimate interaction between infection and obstruction. WANGENSTEEN and BOWERS (cited by BOYD) found that complete obstruction of the infected appendix in the dog always resulted in inflammation, whereas if there was infection without obstruction or obstruction without infection, no inflammation developed.

Furthermore, WANGENSTEEN and BOWERS demonstrated that there was a sphincter-like mechanism at the base of the appendix which made it a potentially closed sac. When a needle was passed through the tip of a normal human appendix at operation and attached to a column of water, not a drop escaped into the cecum at a pressure of 40 cm. Accordingly, it must be presumed that a sphincter-like mechanism exists, and that it may be stimulated to contract by increasing pressure within the lumen.

Our hypothesis is that the pressure within the lumen increases in acute appendicitis; the sphincter mechanism comes into action and thus excludes the influx of any contrast medium into the appendix, even when carboxylmethyl cellulose is added to the medium.

With regard to predisposing causes, it will be sufficient to call attention to the presence of ample amounts of lymphoid tissue and fecaliths, both of which may very well accelerate obstruction.

In chronic appendicitis the healing often results in fibrosis, usually localized to the tip of the appendix. In addition, periappendiceal adhesions may develop, by which the appendix becomes firmly bound.

In chronic appendicitis, the radiologist may therefore expect to find partial filling, cicatricial strictures and, perhaps, a densely adherent appendix.

With regard to the technique used in the examinations reported here the reader is referred to the aforementioned paper on contrast filling of the normal appendix, since we employed the same technique in both cases. The carboxylmethyl cellulose preparation added to the contrast medium, however, was in all cases Cellugel Super 15,000. In none of the cases had the examination to be abandoned on account of nausea, vomiting, etc. The patients were not prepared beforehand; in most cases the contrast meal was given immediately on admission. Roentgenograms were taken at 5, 7, 10, and 24 hours after the ingestion of the contrast meal; in children, an additional examination was carried out as early as after the lapse of 3 hours. At each examination two films were taken, one 18 × 24 cm, without compression, and one 13 × 18 cm, with compression applied gently in view of the danger involved. Furthermore, the abdomen was greatly palpated during the fluoroscopic examination,

by which means we often obtained valuable information as to the site of maximum tenderness.

The case material examined was divided into two groups:

(1) Patients receiving non-operative treatment, and
(2) Patients subjected to operation after the roentgen examination.

Group I

To avoid subjective points of view in diagnosing the cases, we considered only the diagnosis with which the director of the Surgical Department, C. BÜLOW AABERG, labelled the individual case. It should be emphasized that the surgeons did not accept a diagnosis of appendicitis or observation for appendicitis without having elicited definite signs of that condition, and that they did not give consideration to the result of the roentgen examination in making their diagnosis.

The sex and age distribution appears from table 1. Of the 70 patients examined, 41 were women and 29 men. The youngest patient was a 2-year-old girl, the oldest a man, aged 70. The average age for women was 26 and for men 21 years.

Table 1

Sex and age distribution of non-operated patients

Sex	No. of cases	Age, in years				
		0—10	10—20	20—30	30—40	Over 40
F	41	4	15	9	3	10
M	29	9	9	4	2	5
Total	70	13	24	13	5	15

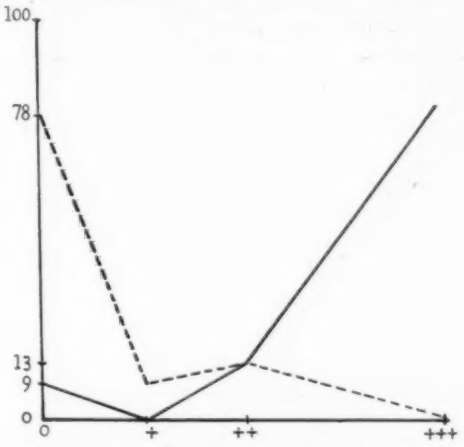
The results of the roentgen examination are seen from table 2; +++ indicates complete filling, ++ partial filling, and + filling at the base.

Table 2

Degree of filling observed in non-operated patients

Degree of filling	No. of cases	Diagnosis on discharge from Department of Surgery			
		Acute app. or obs. f. acute app.	Periapp. abscess	Acute abd. reactions	Other diagnoses
+++	31	0 (0 %)	1	5	25 (78.1 %)
++	13	3 (13.0 %)	1	5	4 (12.5 %)
+	3	2 (8.7 %)	0	1	0 (0 %)
0	23	18 (78.3 %)	1	1	3 (9.4 %)
Total	70	23 (100 %)	3	12	32 (100 %)

Of the 31 patients who showed complete filling, another definite diagnosis such as parametritis, salpingitis, cholecystitis, could be made in 25; on the other hand, none of the patients in whom clinical signs of appendicitis were revealed showed complete filling. A comparison shows that among the 23 patients in whom the appendix failed to fill, 18 revealed definite clinical signs of acute appendicitis. In three patients without clinical signs of acute appendicitis the appendix failed to fill. The cases listed under the diagnosis of peri-appendicular abscess were all patients in whom the attack had passed into a quiescent state and the abdominal mass had subsided. In two patients who showed filling, the appendix had become densely adherent. The 12 cases listed under the diagnosis of acute abdominal reactions were all patients who had had attacks of atypical abdominal pain at home; on admission the pain had completely subsided, for which reason no definite diagnosis could be made.



Graph showing the degree of filling in affected and unaffected appendices. The data from Table 2 have been plotted in a co-ordinate system.

Abscissa: Degree of filling ——— Other diagnoses
Ordinate: Percentage of patients - - - - - - Acute appendicitis

This graph is a graphical representation of the difference in the degree of filling observed in affected and unaffected appendices, the data from table 2 having been plotted in a co-ordinate system.

Group II

In two cases, the patients were subjected to operation 7 hours after the administration of the contrast medium. However, this did not in-

fluence the result of the roentgen examination; at operation it appeared that the contrast medium had passed into the colon, so that there had been an opportunity for the appendix to fill (cf. normal series). In cases in which the diagnosis was unquestionable on admission, and in which immediate surgical intervention was indicated, roentgen examination was not attempted.

The sex and age distribution in Group II appears from table 3. Of the 20 patients examined, 10 were women and 10 men. The youngest patient was a 3-year-old boy, the oldest a woman, aged 49. The average age for women was 22 and for men 24 years.

Table 3

Sex and age distribution of operated patients

Sex	No. of cases	Age, in years				
		0—10	10—20	20—30	30—40	Over 40
F	10	1	6	0	2	1
M	10	2	3	2	1	2
Total	20	3	9	2	3	3

Table 4 shows the results of the roentgen examination and operation. It may here be emphasized that under the diagnoses of acute and chronic appendicitis no cases are listed in which only slight microscopic changes were revealed; in all the cases tabulated, definite macroscopic changes were present. On the whole, greater importance was attached to the macroscopic appearance than to the result of the histologic examination. As appears from the table, contrast filling of the appendix was not seen in any of the cases in which acute appendiceal changes were revealed at operation.

Table 4

Degree of filling observed in operated patients

Degree of filling	No. of cases	Macroscopically or microscopically verified diagnoses		
		Acute appendicitis	Chronic appendicitis	Normal appendix
+++	0	0	0	0
++	1	0	1	0
+	5	0	5	0
0	14	10	4	0
Total	20	10	10	0

Failure of the appendix to fill is not the only feature suggestive of acute appendicitis. The fundus of the cecum is most frequently poorly filled; the mucosal pattern is coarse, and due to edema at the circumference, the junction between the appendix and cecum protrudes in a fashion reminiscent of the portio vaginalis. Figures 1 and 2 are examples of acute appendicitis, whereas figure 3 shows a case of chronic appendicitis.

Two cases are briefly reported below, the first being illustrative of acute, the second of chronic appendicitis.

Report of Cases

Case 1. A man (759/52), aged 41, with a past history of good health without similar attacks, was admitted with abdominal pain. The attack had begun 24 hours previously; at first, the pain was localized to the epigastric region, but later shifted downwards to the right with intermittent exacerbations. Last bowel movement 24 hours before admission; passage of gas 12 hours previously. The pain had been accompanied by slight nausea, and the patient had vomited once. On admission, the patient had only slight pain in the right iliac fossa, no nausea, and seemed relatively well. Temperature 38° C, pulse rate 84; tongue moist.

On deep palpation, slight tenderness was elicited in the right iliac fossa, but otherwise the abdomen appeared soft and normal. Rectal examination revealed no tenderness.

Roentgen examination of the appendix was instituted, and the following report was sent to the Department of Surgery:

"Examination with combined contrast medium with special reference to the appendix showed that the medium had reached the colon 3 hours after the ingestion of the meal. Cecum seemed edematous with relatively coarse mucosal folds and showed only slight filling. The appendix failed to fill. Roentgen diagnosis: Probably acute appendicitis."

The temperature rose gradually, and 12 hours after admission the patient was subjected to operation.

Operative finding: Completely gangrenous appendix without perforation.

Case 2. A man (2521/51), aged 27, was admitted to the Department of Surgery complaining of attacks of non-radiating pain across the abdomen, which had occurred periodically during the previous six months.

Apart from non-paralytic poliomyelitis at the age of 13, his past history was essentially that of good health. He had no pain on admission. A roentgen examination of the appendix was carried out, and our report ran as follows:

"Examination with a combined contrast medium revealed filling of the appendix ten hours after its ingestion. The proximal 2 cm showed filling with a normal lumen; the next 1.5 cm was constricted and thread-like in appearance. The remaining portion of the appendix failed to fill. It was considered that a cicatricial stricture due to a previous inflammatory process was present (Fig. 4). Roentgen diagnosis: Appendix with stricture; observation for chronic appendicitis."

However, the patient was discharged, but was readmitted six weeks later with mild abdominal pain. Physical examination was uncontributory and roentgen examination of the appendix showed completely unchanged conditions. Appendectomy was then performed. The appendix removed was 6.5 cm long; the proximal third was of medium thickness, followed by a portion as thin as a wool thread, while the distal third was completely obliterated. Histologic diagnosis: Sequelae of appendicitis.

Fig. 1. Gangrenous appendicitis in girl, aged 8.

Fig. 2. Acute appendicitis in man, aged 18.

Fig. 3. Chronic appendicitis in woman, aged 22. The appendix, 1—2 cm long, was completely embedded in adhesions. Macroscopically and microscopically, no acute changes.

Fig. 4. Chronic appendicitis in man, aged 27 (case 2).

Discussion

The method described incorporates two new features: a modified technique and the use of carboxylmethyl cellulose added to the ordinary contrast medium. By this method complete filling of the normal appendix may be expected in practically all cases, whereas filling does not occur in acute appendicitis, and typical, easily recognizable changes are visible in the chronic variety. Obviously, this does not infer that the surgeon, with complete assurance, can rely on the result of the roentgen examination and, if the appendix has failed to fill, at once proceed to operate on a patient with acute abdominal pain. Here, as in all other cases, the clinical picture and not a negative finding is of decisive importance. On the other hand, if the clinical diagnosis is doubtful, and a subsequent roentgen examination reveals a well-filled and freely movable appendix, the surgeon may, with equanimity, await further developments. It is particularly in such cases that the method is of value, and this alone is, in fact, a big step forward. Numerous young women with gynecologic complaints and children with indefinite abdominal reactions have been operated on with a diagnosis of appendicitis. In the literature on the subject, it has often been reported that the patients became symptom-free after operation for chronic appendicitis, which strongly suggests that operation was justified, and that the patients had in fact suffered from appendicitis.

Citing VILLUM JENSEN, FELDMAN expressed the view that chronic appendicitis is one of the diagnoses which has led to the largest number of needless operations in the field of abdominal surgery.

MAES claimed that only 15 per cent of the patients operated on for chronic appendicitis are cured, and that failure in the remaining percentage is due to errors in diagnosis.

WHITE reported that misdiagnosis occurs in 50 per cent of all cases.

Anyhow, the percentage of recovery following operation for chronic appendicitis is strikingly low, and it is reasonable to assume that a reliable roentgen examination should result in a considerable change. This assumption is also supported by the fact that among the present series of patients who received operative treatment, not one had a normal appendix; that is to say, not one needless, non-indicated operation was performed.

SUMMARY

A method of roentgen examination of the appendix with addition of carboxylmethyl cellulose to the ordinary barium sulphate meal is reported.

Two series consisting of 70 non-operated and 20 operated patients were examined. In acute appendicitis the appendix fails to fill, whereas the chronic variety reveals either partial filling, cicatricial strictures or, perhaps, complete fixation.

ZUSAMMENFASSUNG

Eine Methode, die Röntgenuntersuchung des Appendix mit Zusatz von Karboxylmethylzellulose zum gewöhnlichen Bariumkontrast auszuführen, wird beschrieben.

Zwei Serien von 70 nicht operierten und 20 operierten Patienten wurden untersucht. Bei der akuten Appendizitis füllt sich der Blinddarm nicht, während man bei der chronischen Form entweder partielle Füllung, Narbenstrikturen oder, vielleicht, vollständige Fixation findet.

RÉSUMÉ

Présentation d'une méthode d'examen radiologique de l'appendice par addition de carboxylmethyl-cellulose à l'habituel repas au sulfate de baryum.

Deux séries de malades furent examinées: l'une de 70 malades non opérés, l'autre de 20 malades opérés. Dans l'appendicite aiguë l'appendice ne se remplit pas, alors que dans l'appendicite chronique il y a soit remplissage partiel, soit rétrécissements cicatriciels ou, peut-être, fixation complète.

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JENSEN, VILLUM: Om Rontgenundersogelse af Appendix. (Danish) Ugeskr. f. læger 101 (1939), 932.

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VOLVULUS OF THE RIGHT COLON

by

J. Frimann-Dahl

The first contributions on volvulus of the cecum appeared about 50 years ago, particularly by v. MANTEUFEL of the Dorpat School as well as by FALTIN and EKEHORN from Finland. Since that time, more than two hundred articles on the condition, mostly from the surgical standpoint, have appeared. Rarely has one author reported more than ten cases of his own.

In his monograph on 'Les volvulus aigus du colon droit' published in 1951, the French surgeon COURTY stated that up till then about four hundred cases were known in the world literature. Publications by radiologists are but few. Eight cases were described by myself in 1943, and seven cases by ABRAMS and WASS ten years later. The condition was also described by MONDOR and PORCHER in 1943 and by MUCCHI and PELLEGRINI in 1948. Thus it has taken a considerable time for radiologists to become interested in the subject. This is, however, to be regretted as the roentgen examination is the only means by which a definite diagnosis may be made preoperatively.

COURTY introduced the term 'volvulus of the right colon'. This seems very reasonable because in most cases not only the cecum is turned or twisted, but also smaller or greater portions of the ascending and transverse colon may be included in the torsion. In this paper these designations will be used alternately. When the ileum and cecum are twisted around each other it seems logical to speak of an ileo-cecal volvulus.

Occurrence

Volvulus of the right colon is a rare but rather interesting lesion producing most characteristic radiologic signs. Without proper treatment,

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which usually means surgical intervention, the outcome is fatal. Correct treatment entirely depends on a definite diagnosis, and this again can hardly be made without an adequate roentgen examination.

As far as is known, volvulus of the cecum occurs in most countries and it is generally accepted that much importance may be attached to the consistency of the food as a causative factor. Food which is coarse, heavy and creates gaseous distension is especially considered to contribute to bringing about torsion and twisting of the colon. In my article of 1943,

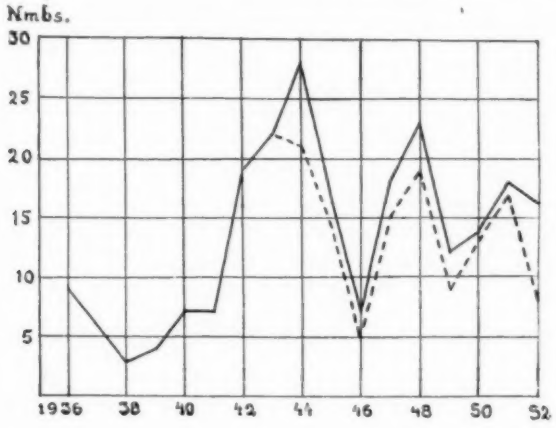


Diagram 1. Occurrence of volvulus of the large bowel. 229 cases, Roentgen Department, Ullevål Hospital. The broken line represents cases on first admission.

I also was inclined to accept this theory without reservation. No doubt, the frequency of volvulus at this hospital increased during the war, when the food situation in Norway was fairly bad. However, under normal conditions during the following years, volvulus still occurred and with about the same frequency. When all cases of volvulus of the large bowel, roentgenologically examined in our department, are listed, we find we have had two hundred and twenty-nine cases during the last sixteen years. Many cases of sigmoid volvulus have been examined several times since the principal treatment consists of the proctoscopic introduction of a rectal tube for deflation of the twisted loop (BRUUSGAARD).

To obtain a correct result of the variations in the number of these cases we have tabulated only patients on their first admission (Diagram 1). The curve shows an increase in the number of patients during 1943—44, the bad times, but the difference during 1947—48 under normal conditions

is very small. On the other hand, the population drawn on by the hospital has increased considerably during the intervening period, so that a proportional increase in the number of patients should have taken place. Therefore, even in a comparatively large number of cases as these, it is rather difficult to draw definite conclusions as to the causal factor of volvulus of the large bowel. It must be considered as natural that the number of cases varies a great deal from year to year. It must also be taken into consideration that in the first years some cases may have been overlooked, and some cases may have been incorrectly diagnosed.

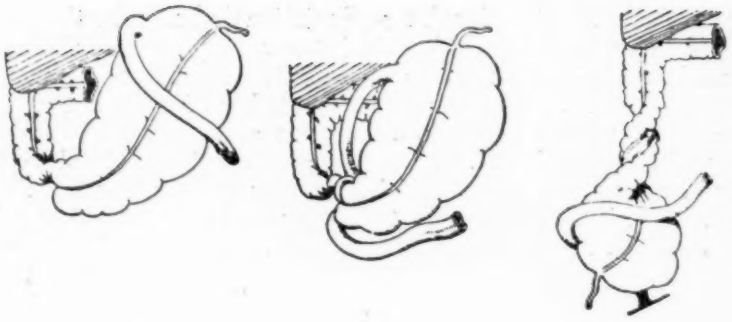
Frequency

Compared to other occlusions of the intestinal tract, cecal volvulus occurs in about five per cent and compared to other instances of volvulus, in about ten to twenty per cent of cases.

Volvulus of the cecum may be found in all ages from the newborn up to 80—90 years. The condition is most frequent in patients between the ages of 20 and 40 years, in contra-distinction to volvulus of the sigmoid which is most often encountered in patients in the 60—70 years age group. It has been indicated that men are more often afflicted with the condition than women. Trauma and violent movements certainly play a part as a causal factor. It is generally considered that many patients with volvulus are imbeciles, or, at least, are feeble-minded. In our material of volvulus of the sigmoid a fair number of such patients have been examined, but the rule does not seem to be valid as far as volvulus of the right colon is concerned. Finally, it should be mentioned that volvulus of the cecum may occur in rare instances during pregnancy. However, we have had no such cases in our series.

Pathogenesis

In volvulus of the cecum, various congenital malformations may be found and these are often essential for the development of the lesion. In order to understand these anomalies thoroughly, we must remember how the development of the intestinal tract and rotation of the large bowel takes place. The migration of the colon from the left to the right starts in the second to third month of fetal life and is generally completed in the eighth month. Abnormalities in rotation may be followed by non-fixation or displacement of the cecum. Failure in rotation may also result in an abnormal shape and mobility of the mesentery — in a mesenterium ileocolicum commune. Such a malformation is frequently observed in cases of volvulus of the cecum (JAKOBSEN). However, the cecum may be mobile even without this anomaly and it has been estimated at autopsy that in



a. b. c.

Fig. 1. Types of volvulus according to COURTY. a) Ceco-colic, b) Ileo-ceco-colic, c) Axial torsion.

about ten per cent of specimens the cecum is so movable that torsion seems to be possible. Now, as a volvulus of the cecum is not as frequent as this, other pathogenetic factors must be searched for. The main point is that the mesentery must be long and band-like with a pediculated fixation to the posterior wall. This is often carried to excess in the actual torsion.

COURTY has pointed out that a band-like adhesion is frequently observed at the fundus of the cecum in cases of volvulus. Fixed by this band, the cecum may be liable to turn or twist (Fig. 2 c).

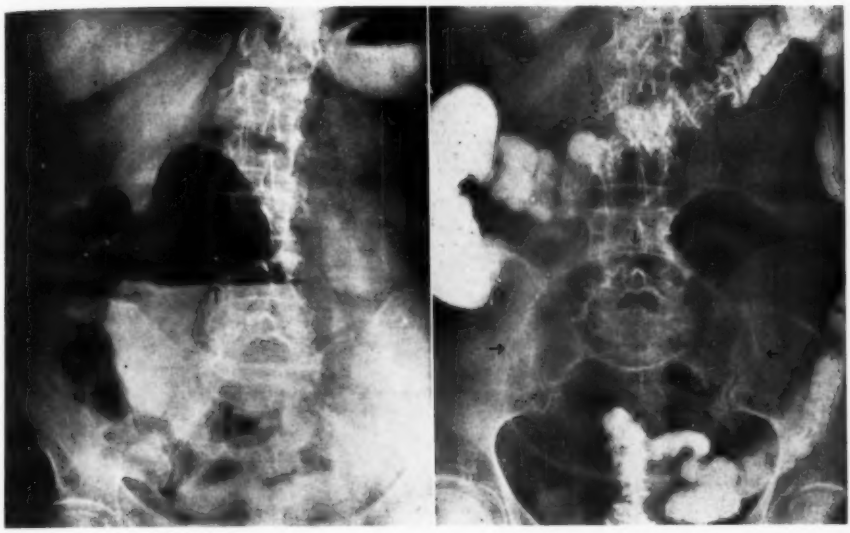
TORGERSEN has mentioned a relationship between cecal volvulus and nterposition of the colon (the right flexure). This material has given no support for such a conjecture.

Classification

FALTIN grouped volvulus of the cecum into two different types:

1. the sack type in which the colon shows an axial torsion and
2. volvulus of the loop type in which part of the ileum is twisted around the colon. This grouping would be valuable if volvulus of the sack type gave rise to clinical signs similar to those of a simple occlusion and the loop type to those of a strangulating obstruction. This, however, is not always the case. The various types may also be encountered simultaneously and an exact classification may be impossible or merely a matter of individual conjecture. COURTY divided volvulus of the right colon into three types:

1. ceco-colic,
2. ileo-ceco-colic, and
3. axial torsion. This latter type seems to be similar to the first (Fig. 1).



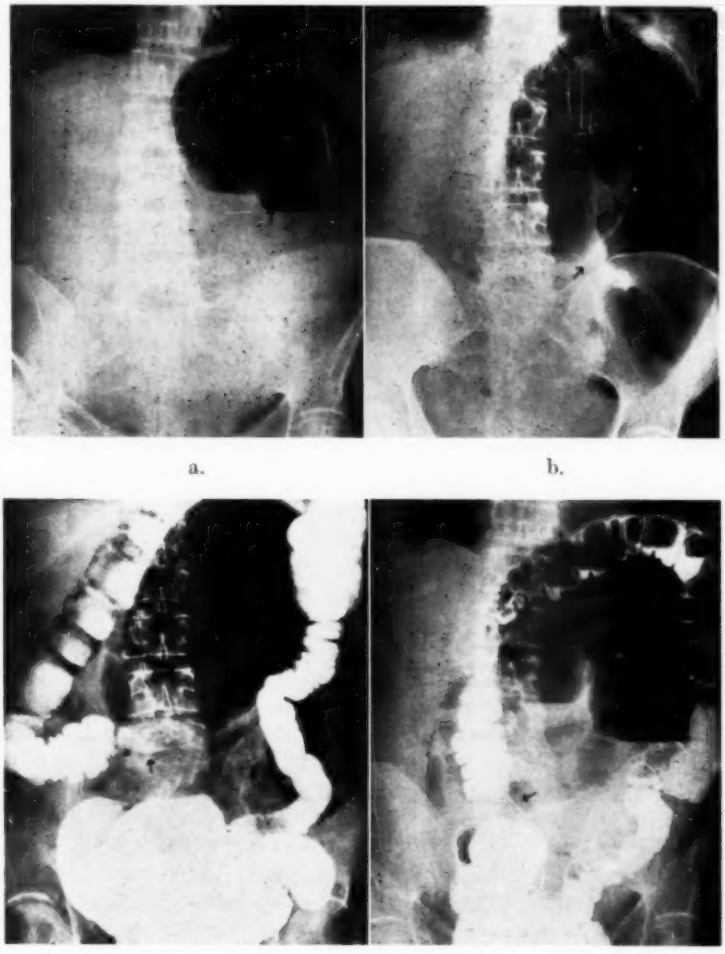
a. b.

Fig. 2. a) Upright position. Fluid level in the inflated cecum. Gas-filled ileal loops laterally to the cecum. — b) In supine position after evacuation of the barium enema: Cecum visualized as a cyst-like formation in the pelvis. Note difference of site after change of posture.

The torsion is most often 180°—360°, and a clockwise turn is more frequent than in the opposite direction. JAKOBSEN, in one case, observed a torsion of 720° (a complete double torsion). The mortality rate after reduction or resection seems to be about twenty-five per cent.

Clinical Diagnosis

Clinically the lesion is very difficult to diagnose, and most authors admit a correct preoperative diagnosis is exceptional. A mechanical occlusion or a volvulus may be suspected but to decide whether the twisted loops consist of the sigmoid or cecum ascendens is, as a rule, impossible. In general, two main signs are mentioned: 1, a distended and palpable fundus of the cecum (v. Wahl's sign), and 2, an empty right iliac fossa. An old and well-known procedure is to give an ordinary water enema. If this returns quickly the stenosis must be in the distal portion of the large intestine, whereas if most of the fluid is retained a torsion in the cecum is more likely. The barium enema has rendered such an examination almost superfluous. The clinical diagnosis is often that of mechanical ileus or

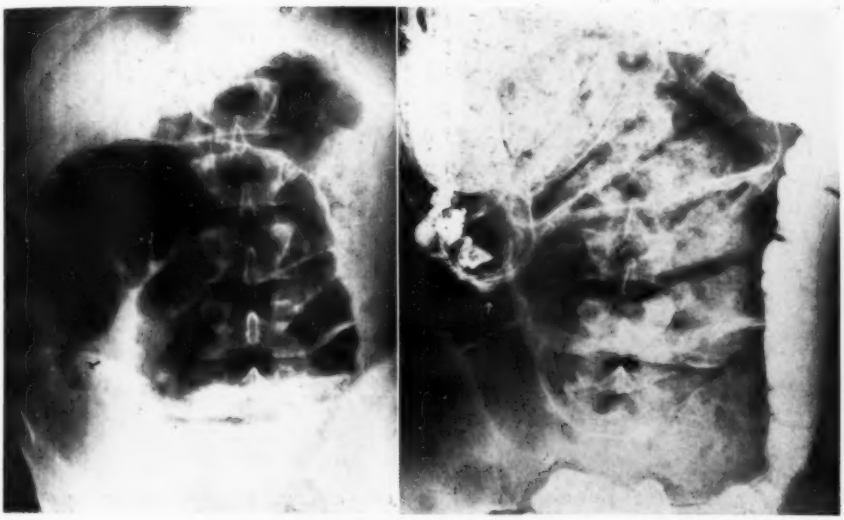


a. b.

c. d.

Fig. 3. (a and b) Cecum situated upwards and to the left. Cecum volvulus in supine and erect position, arrow pointing towards the root of the mesentery. — c) After barium enema, the column of contrast medium is tapered; end points toward the distended bowel. — d) Note value of taking films in upright position after evacuation of the barium enema.

acute appendicitis. The distended cecum displaced down in the minor pelvis may easily be mistaken for a twisted ovarian cyst. Changes of posture during the roentgen examination should prevent such misinter-



a. b.

Fig. 4. Cecum volvulus. — a) Erect position. Gaseous distension of the cecum and part of the ascending colon. No fluid level. Note spur-like off-shoot corresponding to the torsion. — b) Barium enema shows twisted relief at the site of the torsion.

pretation as it will reveal the mobility of the distended cecum (Fig. 2). Years ago, two of our cases with erroneous diagnoses were examined only by urography because the clinical diagnosis in each case was that of acute ureteral stone.

The Roentgen Diagnosis

Based on a complete roentgen examination, the diagnosis is comparatively easy, but may on the other hand in some instances be rather tricky. Even the ordinary films may give definite grounds for the diagnosis. Demonstration of the distended cecum is essential. Practically, this may be found in any situation in the abdomen, but is most often seen to lie in the epigastrium and the left hypochondrium (Fig. 3). Fluid levels may be demonstrated in the descended cecum; usually one long level is seen if the sack type is present, and two levels if the torsion is of the loop type. In this latter case, the findings are often similar to those of a volvulus of the sigmoid in which two fluid levels are also visible, one in each limb of the loop. In some rare instances, the cecum is mainly filled by fecal masses so that no fluid level can be demonstrated (Fig. 4 a, b). It has also been proven by the barium enema that the tapered end of the

a.

c.

b.

Fig. 5.

a) Volvulus of the right colon, upright (360° clockwise turn). Fluid levels in terminal ileal loops.

b) Barium enema stops at the site of torsion; converging small bowel loops.

c) After evacuation, torsion relief corresponding to the block. Distended cecum in the left flank.

twisted loop may be observed directly on the survey film as a small spur-like off-shoot. In most cases of cecal volvulus, the small intestine (ileum) also is involved and shows signs of occlusion and retention of gas and fluid; small fluid levels are apparent if a horizontal projection of the roentgen beam is employed (Fig. 5). This is an important differential point, for in sigmoid volvulus there are usually no signs of distended small bowel loops except when peritonitis complicates the condition.

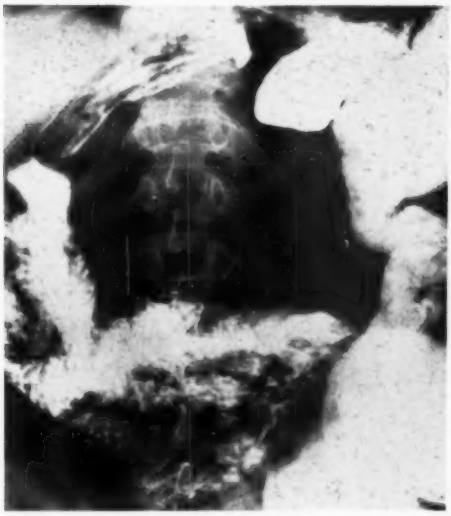


Fig. 6. Enormously distended cecum in the epigastrium displacing the stomach upwards. Barium enema and meal.

In volvulus of the sigmoid the sign is accentuated so that in the supine position a band-like density, produced by the double wall of the twisted loop, is visible stretching down towards the site of the torsion, which usually is situated in the left iliac fossa. A small tumour-like mass, corresponding to the mesenteric root is visible, so that the appearance resembles an inverted comma. In this material of cecal volvulus a similar finding was detected only once.

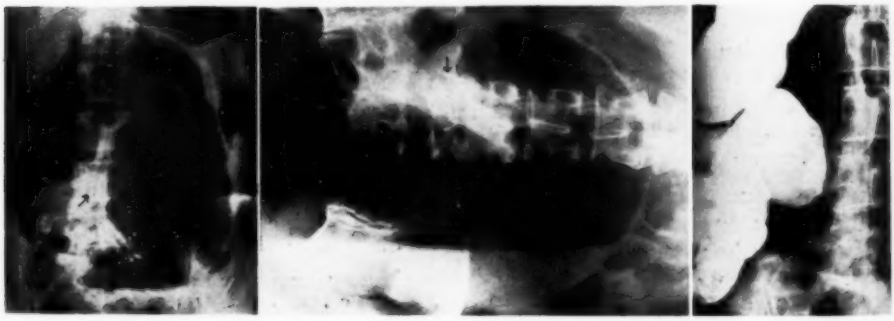
In the lateral decubitus position, one long fluid level may be seen in the distended loop and the distended small intestinal loops are also well shown. In some of our cases additional films obtained in the supine position with a horizontal projection have been of value.

The cecum, if distended, may encroach upon adjacent organs such as the stomach, duodenum or splenic flexure of the colon. This is readily revealed by a barium meal or enema (Fig. 6). If the cecum is displaced downwards into the minor pelvis, the bladder may be compressed.

The decisive findings are generally made by means of the barium enema. The column of contrast medium stops at the site of torsion and has a tapered outline, and at times a torsion relief, which always points toward the stenosis and the inflated cecum (Fig. 7). In other instances, the loops may be so firmly twisted that no barium enters the twisted bowel (Fig. 8). In such cases, the distended cecum (and cecum ascendens)

a. b.

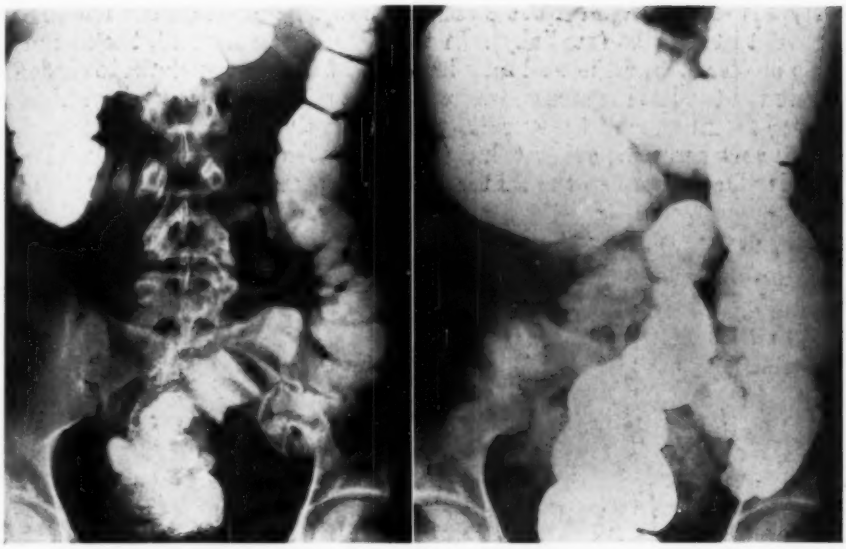
Fig. 7 a) Upright position. Distinct fluid level in the cecum (arrow); also distended ileal loops (to the right). — b) Torsion of the cecum (360°). Barium enema. Arrow pointing at the tapered end corresponding to the torsion.



a. b. c.

Fig. 8. a) Cecum volvulus. Upright position. Arrow pointing at the mesenteric root. — b) Left side down. Long fluid level in the cecum. — c) Barium enema. Complete block at site of torsion.

may closely simulate a distended sigmoid. However, the 'open' medial contour and the density corresponding to the mesenteric root should prevent misinterpretation (see later).



a. b.

Fig. 9. Cecum volvulus — possible axial torsion. — a) Barium enema shows site of the stenosis. — b) After renewed injection, filling of the cecum. Reduction.

In cases of axial torsion, reduction may take place spontaneously or during the barium enema. It is important to remember this because during the procedure, the radiologist may facilitate the reduction by palpation or turning the patient into various positions (Fig. 9).

The material now comprises twenty-three cases covering ages varying from seven days to 82 years, but mostly lying in the 20—40 years group. Men and women were about evenly divided. Five of the cases died, giving a mortality rate of about 23 per cent; this is comparatively low.

One definite diagnostic error was made in a newborn child admitted with the diagnosis of 'peritonitis'. Volvulus of the cecum was not mentioned at all in this case. Experience has thus taught one that even in small children the possibility of a cecal volvulus should be considered. No other diagnostic mistake has been made during the last few years.

Differential Diagnosis

1. *Volvulus of the sigmoid.* This is often suspected but the differentiation may be readily decided by means of a barium enema. On examining the ordinary films taken in the supine position, one should think of a

volvulus of the cecum if the distended bowel situated on the left side, is 'open' to the right (medially). In volvulus of the sigmoid, the distended loop is 'closed' and the wall may be followed all the way down towards the torsion in the left iliac fossa, where the root of the mesentery (mesosigmoideum) forms a small tumour-like mass. In volvulus of the cecum similar appearances may be evident, but the root of the mesentery is much larger and is placed more to the middle of the abdomen (Fig. 10). Another im-

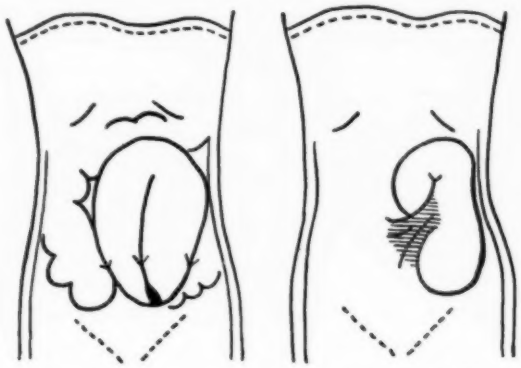


Fig. 10. Representation showing difference between sigmoid and cecum volvulus.

portant point is that in volvulus of the sigmoid the remainder of the large bowel is more or less distended by gas and in the erect position shows fluid levels. In volvulus of the cecum part of the colon distal to the stenosis is often devoid of gas and fecal matter, but may on the other hand in some cases show signs of slight distension. Torsion simultaneously of both the sigmoid and the right colon must be considered extremely rare.

2. *Volvulus of the small intestine.* During the same period we have tabulated five hundred and twelve cases of small intestinal obstruction and twenty-eight have been listed as volvulus of the small bowel. Only cases in which a torsion of a smaller or greater portion of the intestine has been the primary cause of the condition have been diagnosed as volvulus. In some rare instances, the twisted loop was greatly distended and approximated in size to a moderately distended colon. However, clinically the loop is palpable only in extremely rare cases and cannot definitely be identified as part of the small bowel. The roentgen findings in volvulus of the small intestine exhibit many variations according to the size and site of the twisted coils. The involved loops are usually distended by gas and the mucosal pattern may reveal the presence of edema. Only occasionally is the loop so increased in size that one is led to suspect a volvu-

Fig. 11. Volvulus of the small bowel. Considerable distension of the affected loop (360°).

Fig. 12. Large bowel obstruction due to small growth of the sigmoid. Mobile cecum, considerably distended, showing fluid level in erect position.

lus of the cecum (Fig. 11). It must be emphasized that in strangulation obstruction the afflicted loop is not inflated but is filled only with fluid. A kind of valve mechanism must therefore have developed in a volvulus, contrary to the mechanism in strangulation obstruction in which the obstruction is complete (incarceration). In a volvulus of the cecum, the gas may enter the loop but cannot escape in the anal direction. A hindrance to the passage is produced by the torsion and consequently no gas will accumulate in the remainder of the large bowel.

3. *Large bowel obstruction.* If the stenosis is situated on the left side, the cecum may be enormously distended, giving rise to suspicion of a volvulus of the cecum. However, gaseous distension of the colon down towards the stenosis should prevent misinterpretation and a barium enema will in most cases give confirmatory evidence of a simple occlusion and may, sometimes, reveal a small cancer of the sigmoid as the primary lesion (Fig. 12).

4. *Knot formations.* This is a very rare condition. In our material we have collected three cases examined roentgenologically. The author described the signs in 1942 and since then no publications seem to have appeared. Most often, the ileum twists around the sigmoid, which must be long and have a tendency to form a hoop or a hair-pin turn. When the

a. b.

Fig. 13. Knot formation. — a) Supine. Gas-filled twisted sigmoid and ileal loops in 'rosette-like' arrangement. — b) Barium enema stops at site of the knot, showing characteristic indentation corresponding to the turning of the ileal loops.

formation of the knot is complete a stenosis is established both in the ileum and in the sigmoid (Wilms). The trunk-shaped tapering of the barium enema at the site of the stenosis and a left-sided indentation corresponding to the turning axis of the ileal loops is most characteristic (Fig. 13).

5. *Dilatation of the stomach.* At times a distended and displaced cecum may be confused with a dilated stomach. Administration of a barium meal may be necessary to detect gastric displacement; the stomach may lie medial to the cecum. In making the diagnosis, the possibility of a volvulus of the cecum should be kept constantly in mind. The ordinary films may give good grounds for a suggestion of a torsion, but the barium enema is the decisive diagnostic procedure.

SUMMARY

The author reviews the roentgenologic signs of volvulus of the right colon (volvulus of the cecum) based on a material comprising twenty-three cases. A distended and displaced cecum with gas-filled small intestinal loops showing fluid levels are characteristic. The barium enema is decisive, the contrast medium stopping at the site of torsion and showing a twisted and tapered end which points towards the distended cecum. A short discussion of the differential diagnosis is given.

ZUSAMMENFASSUNG

Unter Bezugnahme auf ein Material von 23 Fällen von Volvulus in dem rechtsseitigen Dickdarmabschnitt (Volvulus des Caecum) gibt der Verfasser eine Übersicht über die röntgenologischen Kennzeichen dieser Erkrankung. Ein ausgespanntes und verschobenes Caecum mit luftgefüllten Dünndarmschlingen, die Flüssigkeitsspiegel aufweisen, sind charakteristisch. Der Bariumeinlauf ist entscheidend; die Lage der Stenose wird durch Obstruktion des Kontrastmittels angegeben, der Kopf der Kontrastsäule ist verzerrt und ihr schmaler werdendes Ende gegen das ausgespannte Caecum gerichtet. Die Differentialdiagnose wird kurz besprochen.

RÉSUMÉ

Se basant sur vingt trois cas de volvulus du colon droit (volvulus du caecum) l'auteur décrit les signes radiologiques de cette affection. Un caecum distendu et déplacé et des anses grêles remplies de gaz et présentant des niveaux liquides sont caractéristiques. Le lavement baryté emporte la décision, le siège de la sténose est signalé par l'arrêt du lavement opaque, la tête de la colonne est tordue et son extrémité effilée est dirigée vers le caecum distendu. Le diagnostic différentiel est brièvement discuté.

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Addendum

While in press an article on volvulus of the cecum by Figiel appeared in Radiology 61 (1953), 496.

FROM THE 1ST ROENTGEN DEPARTMENT (DIRECTOR: DOCENT GUNNAR JÖNSSON), SÖDERSJUKHUSET, STOCKHOLM, SWEDEN

ANOMALOUS PULMONARY VEIN ENTERING THE INFERIOR VENA CAVA EXAMINED BY SELECTIVE ANGIOCARDIOGRAPHY

by

H. Arvidsson

Pulmonary veins entering the right auricle or its tributaries were described by the anatomist WINSLOW, as early as 1739, although interest in these malformations was at that time a pure anatomic one. With the development of thoracic surgery and with it the possibilities of correcting anomalies of the thoracic circulation, a desire has been expressed by surgeons for the diagnosis of such anomalies during life.

The simplest and safest way to a correct diagnosis of an anomaly of the pulmonary circulation is angiocardiography combined with catheterization and blood gas analyses. This method has been used in such cases by, inter alios, DOTTER and STEINBERG, SNELLEN and ALBERS, and GRISHMAN, BRAHMS, GORDON and KING.

There are two main types of anomalous communication between the pulmonary veins and the right auricle.

1) Pulmonary veins entering a persistent left superior vena cava. The passage to the right auricle then goes via a left innominate vein or via the coronary sinus.

2) Entrance of pulmonary veins to the superior or inferior vena cava or directly to the right atrium.

An excellent review of the present conception of the embryologic problems concerning these malformations was made by HEALEY in 1952. During early embryologic life the primary pulmonary plexus has connections with the cardinal veins, which form the adult caval system. The anomaly to be described may be explained by a persistence of this vas-

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cular communication. Several other malformations of the pulmonary veins may be analyzed embryologically in a similar way, but they will not be discussed here.

Patho-physiologically the anomalous inflow of the oxygenated blood from the lungs into the right side of the heart means a left-to-right shunt. Part of the blood moves circuitously through the lungs and the right side of the heart. This increases the blood volume passing through the lesser circulation, a fact that is demonstrated by increased vascular filling of the lungs and dilatation of the right side of the heart. Furthermore, the systemic circulation is deprived of part of the oxygenated blood coming from the lungs. This forms the explanation to the main clinical manifestation of the anomaly, viz. a decreased cardiac reserve. In uncomplicated cases with partial anomalous drainage, no cyanosis appears.

The degree of shunting partly depends on how great a portion of the lungs is drained to the right side of the heart. In cases where all the pulmonary veins enter the right auricle or its tributaries, the systemic circulation depends on a right-to-left shunt, *i. e.* an auricular septal defect or sometimes a patent ductus arteriosus. In such cases the capacity of the septal defect or the patent ductus determines the degree of shunting. Cases with combination of these anomalies and a long survival time are described by SNELLEN and ALBERS. HUGHES and RUMORE claim that some 50 % of the systemic blood may be shunted back to the lungs without obvious symptoms.

The present case is that of a male, aged 37, with very slight cardiac symptoms of dyspnea, palpitations and vertigo after exercise. The symptoms had gradually increased. Physical examination showed moderate bulging of the precordial area to the right. On auscultation the first heart sound was doubled in the right second and third intercostal spaces, and the second sound accentuated. Regular rhythm, no murmurs. Blood pressure 125/75. No cyanosis, no clubbing of the fingers.

Conventional chest roentgenograms (Fig. 1) show a displacement of the heart to the right. The volume determination was uncertain because of this displacement and a rotation of the heart but was calculated as being 700 cc corresponding to 350 cc per square meter body surface. The vascularity of the lungs is moderately increased. In the right lung, there are wide vessels running in a curved downward course following the right cardiac border. During fluoroscopy no pulsations were seen in the vessels.

Angiocardiography. A catheter no. F. 12 was inserted so that the tip was situated in the main stem of the pulmonary artery during the injection (Dr. KARNELL). It was found impossible to enter the right main branch of the artery. 90 cc of Umbradil 70 % (3.5 di-iodo-4-pyridone-N-acetic-dietanolamine) solution was injected in 2.5 secs. 20 films in all were obtained both in frontal and lateral projections during 8 seconds (JÖNSSON, BRODÉN and KARNELL). In the arterial phase (Fig. 2) normal lung arteries are clearly visible in both lungs. In the venous phase (Fig. 3) no normal pulmonary veins are evident in the right lung, but in the lower part, corresponding to the findings in the conventional radiograms, wide irregular filled vessels are seen. It is clearly evident that they coalesce to form a single large vein which enters the inferior vena cava. There was no obvious

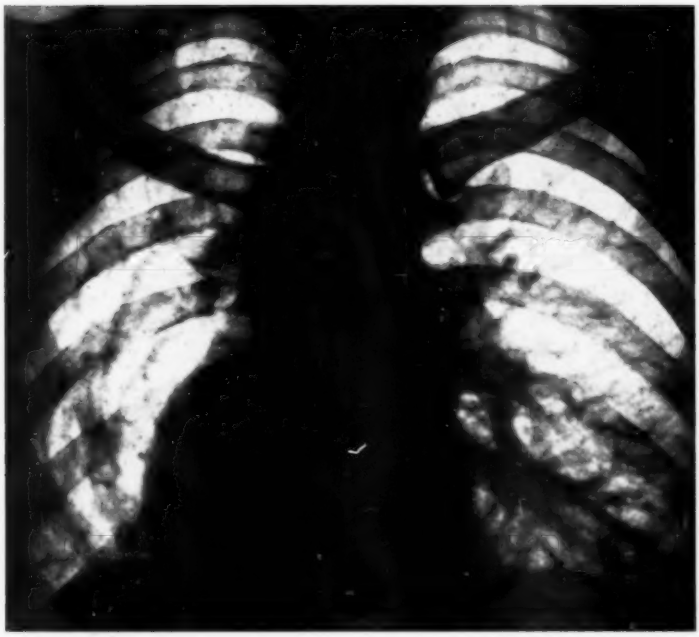

Fig. 1. Chest radiogram, frontal view. Pathologic veins are visible in the right lung, following the cardiac border.

discrepancy between the circulation time of the right and left lung. The results of blood gas analyses and pressure measurements are shown in Table I. In order to determine the respiratory capacity of the abnormal lung, bronchospirometry was carried out (Dr RICHTNÉR) and the results are shown in Table II. The figures show clearly that besides the fact that the vital capacity is low, the efficiency of the right lung as a respiratory organ is only some 50 % of that of the left. A lung with the described anomaly is thus alone probably incapable of maintaining the arterialization of the blood.

Table I

Blood gas analyses

	Volume% oxygen	Oxygen saturation
Sup. v. cava	12.4	69.9
Right auricle	13.8	77.4
Inf. v. cava	16.6	93.1

Pressure measurements

Right ventr.	12 cm of water
Pulm. art. main stem	18 cm of water
Pulm. art. left branch	15 cm of water
Pulm. art. right branch	12 cm of water

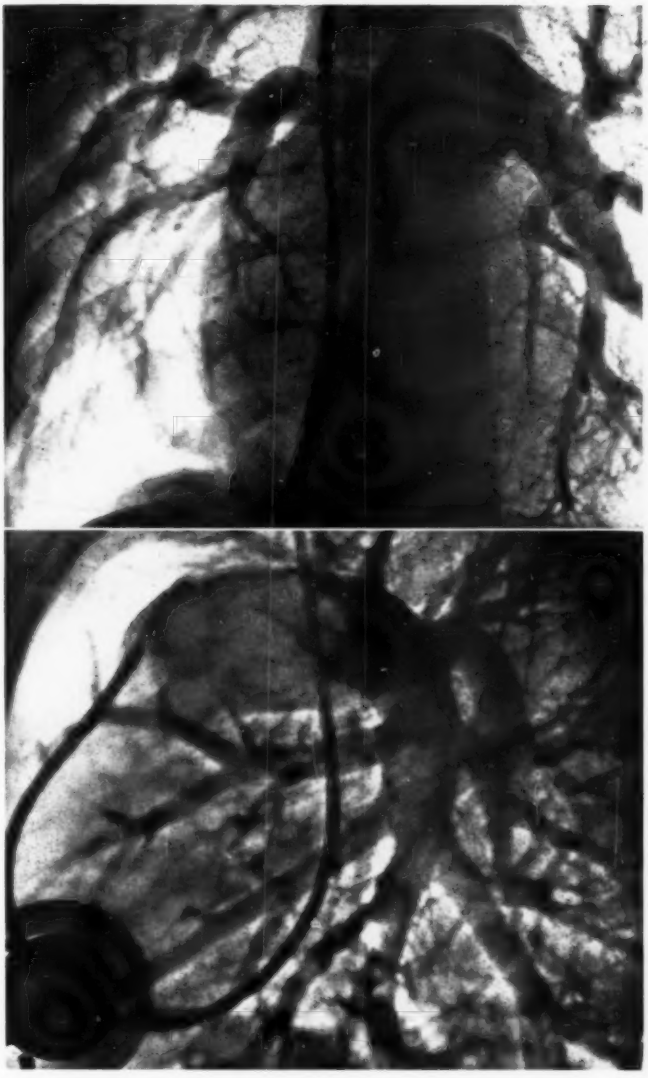

Fig. 2. Angiocardiography, arterial phase. Frontal view (top): The tip of the catheter is seen in the main stem of the pulmonary artery. Lateral view (below): Normal pulmonary arteries.

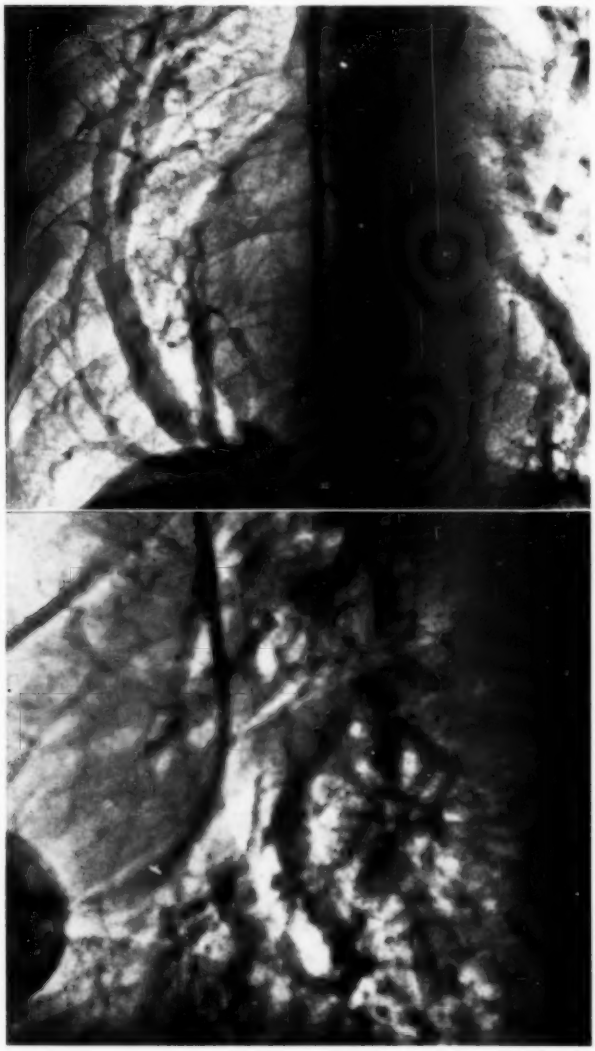

Fig. 3. Angiocardiography, venous phase. Frontal view (top): Pathologic veins in the right lung contrast filled. Lateral view (below): The pathologic veins are not well seen, because of the superimposed left pulmonary veins.

Table II

Bronchospirometry

a) *Rest*	Right lung	Left lung
O_2-uptake litre/min.	138	212
minute ventilation cc	3,420	2,520
ventilation equiv.	2.4	1.2
tidal air cc	190	140
complemental air cc	310	520
reserve air cc	100	60
vital capacity cc	600	720

b) *After exercise 596 kp during 5 minutes*

	Right lung	Left lung
O_2-uptake litre/min. cc	206	408

The case presented shows almost identical patterns to those described by SNELLEN and ALBERS, FINDLAY and MAIER, DOTTER and STEINBERG and others. It must be emphasized that this is a typical malformation and it is generally possible to establish the correct diagnosis from conventional chest roentgenograms. It must, however, be pointed out that in several cases described in the literature the anomaly coexists with other malformations of the heart. In doubtful cases, therefore, it is advisable to employ angiocardiography, preferably the selective method which gives more precise anatomic information, combined with catheterization and blood gas analyses.

SUMMARY

The author describes a case with an anomalous pulmonary vein entering the inferior vena cava. The findings in conventional chest roentgenograms and selective angiocardiography as well as the results of blood gas analyses and bronchospirometry are discussed.

ZUSAMMENFASSUNG

Der Verf. beschreibt einen Fall mit einer Anomalie der V. pulmonalis, die in die V. cava inf. mündet. Die Befunde auf den üblichen Röntgenfilmen des Thorax und bei der selektiven Angiokardiographie sowie die Ergebnisse der Blutgasanalysen und der Bronchospirometrie werden besprochen.

RÉSUMÉ

L'auteur décrit un cas de veine pulmonaire anormale se jetant dans la veine cave inférieure. Il étudie les images sur les radiographies simples du thorax et sur les angiocardiographies sélectives ainsi que les résultats des analyses des gaz du sang et de la bronchospirométrie.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR TORLEIF DALE),
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RADIOLOGIC FINDINGS IN INJURIES OF THE FINGERS

by

Erling Kierulf

Injuries of the fingers are a comparatively common occurrence. According to statistics (ZIEGLER, POMETTA and ZOLLINGER), sprains constitute about ten per cent of all traumatic injuries. The distribution of sprains involving the upper and lower extremities is as follows: Ankle 38 %; Wrist 21 %; Knee 16 %; Fingers 13 %.

In textbooks a differentiation is usually made between distortion or sprain and contusion. A distortion or sprain may be defined as a wrenching of a joint out of its natural or normal position, brought about by momentary violence. Excessive, adventitious stress on a joint will therefore result in a sprain. The momentary, forcible overstretching will give rise to a partial or complete rupture of the joint capsule or ligaments. Overstretching of particularly strong ligaments may result in a tearing of the tendon insertion into the bone instead of rupture of the ligament.

Contusion of a joint is a direct result of the traumatic action of an injury to the soft tissues adjacent to the joint, *i. e.*, skin, subcutis, muscles, ligaments, fascia, and joint capsule. It is accompanied by extravasation of blood into the tissues involved. If the synovial membrane is seriously injured, hemarthrosis will usually occur, but as against a distortion, the ligaments will not be ruptured. Contusion of a joint, however, is frequently coupled with a distortion.

Finger injuries are frequently referred for radiologic examination. Attention is primarily paid to fractures, either in the form of a simple fracture or of a tearing of the tendon insertions.

In recent finger injuries not associated with fractures, I have never observed any pathologic changes of the bony structures. Swellings of soft tissue naturally stood out clearly. This agrees with the observations

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a. b. c.

Fig. 1. Injury to right middle finger six months prior to examination. (a) Swelling of soft tissue, combined with calcification. Small marginal defect of middle phalanx. (b) Radiograph six years later showing persisting small defect in the middle phalanx. (c) Semilateral view of same.

a. b c.

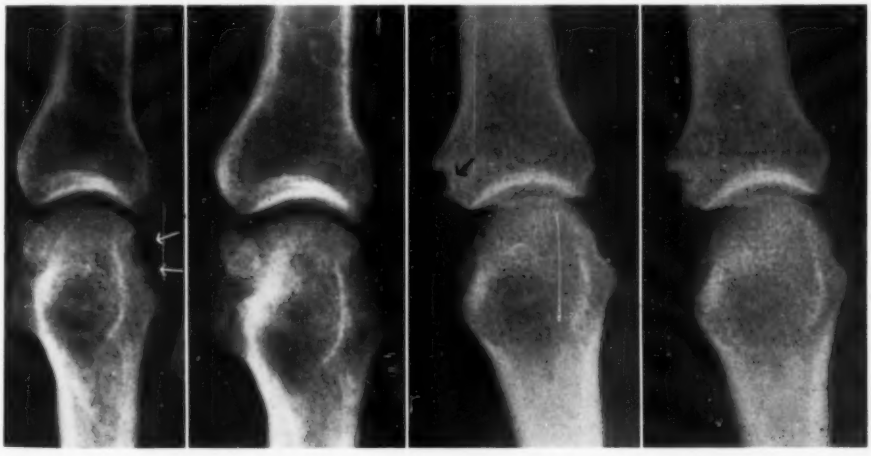
Fig. 2. Distortion of right middle finger three months prior to examination. (a) Marginal defect on ulnar border of base of phalanx and punched-out defect in proximal ulnar and volar aspect of middle phalanx. (b) Semilateral view of same. (c) Radiograph eight years later. Defects somewhat smaller but not completely healed.

recorded in the textbook of SCHINZ, BAENSCH, FRIEDL, and UEHLINGER: "A distortion produces no radiographic characteristics because there is no injury of the bony structures but of the soft tissues only. Marked swelling and intra-articular extravasation will appear as a widening of the contours of the soft tissues. Serious sequelae of contusion are chipping

3 a. 3 b. 4 a. 4 b.

Fig. 3. Injury to the right thumb three months prior to examination. (a) Marginal defect of the distal dorsal aspect of metacarpal bone. (b) Radiograph six years later showing healing of defect.

Fig. 4. Injury to the left thumb two months prior to examination. (a) Punched-out marginal defect of the volar proximal portion of proximal phalanx. (b) Radiograph two-and-a-half years later, showing partial healing of defect.



5 a. 5 b. 6 a. 6 b.

Fig. 5. Injury to third metacarpophalangeal joint of middle finger eight months prior to examination. (a) Marginal defect of the ulnar distal portion of third metacarpal bone. (b) Radiograph three-and-a-half years later, showing partial healing of defect.

Fig. 6. Injury to right index finger six months prior to examination. (a) Marginal defect of radial proximal portion of proximal phalanx. (b) Radiograph ten months later, showing partial healing of the defect (note sharp sclerotic marginal zone).

a. b. c. d.

Fig. 7. Injury to the right third finger three weeks prior to examination. (a) Normal bone, swelling of soft tissue. (b) Radiograph six months later, showing small defects at the distal portion of proximal phalanx. (c) Radiograph nineteen months after injury showing the defects with sharp sclerotic marginal zone. (d) Semilateral view of same.

of the bone and subchondrous extravasation of blood which may interfere with the nutrition of the bone and lead to subsequent sequestrum formation."

In cases of distortion and contusion of interphalangeal or metacarpophalangeal joints I have frequently observed skeletal changes in radiographs taken some time after the injury. The symptoms, which in these patients had lasted for at least two months, consisted of swelling of the joint with painful and a somewhat limited movement. Similar changes were observed in a case of dislocation of an interphalangeal joint, where the dislocation had been reduced immediately after the injury. Swelling, however, persisted, for which reason the joint was examined radiographically three weeks after the injury.

The skeletal changes observed are localized to the joint area of the bones. They show considerable resemblance to the punched-out defects, marginal tophi, occurring in arthritis urica. The changes may be easily overlooked unless due care be exercised.

In twenty patients control radiographs were taken up to several years after the injury. The changes observed were fairly identical in the different cases.

The defects presumably appear some time after the injury, as I have never observed similar defects in radiographs obtained immediately following it.

Fig. 8. (From Spalteholz.) Showing the anatomy of the joint capsule and the collateral ligament.

How can these changes be explained? As any form of fracture may be excluded, I personally consider the changes to be due to vascular disturbances. The injury has affected only the joint capsule or ligaments and not caused complete rupture which would have given rise to severe clinical symptoms including abnormal mobility.

In figure 8 which shows the ligaments and capsules of the metacarpophalangeal and interphalangeal joints, the capsule as well as the ligaments is seen to join the periosteum close to the articular surfaces. The strong collateral ligament of the metacarpophalangeal joint runs in a slightly oblique direction, while those of the interphalangeal joints run parallel to the long axis of the finger. Vascular damage resulting from injury to these structures may possibly give rise to localized ischemia which in turn — according to its severity and duration — may cause necrosis of the dependent area of the bone. As shown by the radiographs,

the defects may occur on either side of the joint, or on both sides simultaneously, always corresponding to the capsule or the insertions of the ligaments.

SUMMARY

Traumatic osseous changes localized to the joint area of the fingers are described. About two months after an injury small punched-out defects may occur resembling marginal tophi in gout. These changes were controlled by roentgen examinations for several years after the trauma.

ZUSAMMENFASSUNG

Traumatische Knochenveränderungen in der Fingergelenkgegend werden beschrieben. Etwa 2 Monate nach einem Trauma können kleine ausgestanzte Defekte auftreten, die marginalen Gichtknoten ähneln. Diese Veränderungen sind durch Röntgenuntersuchungen mehrere Jahre nach dem Trauma kontrolliert worden.

RÉSUMÉ

L'auteur décrit des lésions osseuses traumatiques localisées aux régions articulaires des doigts. De petites pertes de substance à l'emporte-pièce, ressemblant aux tophi marginaux de la goutte peuvent apparaître environ deux mois après un traumatisme. Ces lésions ont été contrôlées radiographiquement pendant plusieurs années après le trauma.

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FROM RADIUMHEMMET (DIRECTOR AT THE TIME OF THE INVESTIGATION: THE LATE PROFESSOR HUGO AHLBOM), STOCKHOLM, SWEDEN

TREATMENT OF CARCINOMA OF THE THYROID

by

Folke Jacobsson

Our knowledge of the histology, clinical behaviour and natural duration of carcinoma of the thyroid has been considerably increased during the last few years (DOBYNS and LENNON 1952, FRAZELL and FOOTE 1949, HARE and SALZMAN 1950, WARD 1949, inter alios). The interest in this tumour has been great. Since it has become possible to treat certain cases of cancer of the thyroid with metastases with radio-active iodine, the interest has become enormous.

There still remains marked uncertainty as to the value and the indications for radiotherapy in thyroid carcinoma. The highly differentiated adenocarcinomata of the thyroid, with the exception of the papillary adenocarcinomata, appear to be fairly radioresistant. This radioresistance may, however, only be apparent. It is in connection with the advanced inoperable cases that this matter of course generally arises, by reason of the fact that it has not been found possible to give both a homogeneous and sufficiently high tumour dose to the whole anatomic extent of the tumour without the tolerance dose for the surrounding uninvolved tissue being exceeded. To this must be added the difficulties of assessing the results of radiotherapy, caused, among other things, by the extremely slow course of many cases of carcinoma of the thyroid, both as regards the primary tumour and the metastases. FRAZELL and FOOTE have described a case of carcinoma of the thyroid with the patient living and without symptoms twenty-two years after thyroidectomy, and thirteen years after the onset of bone lesions. WARD has followed another case in which multiple lung secondaries remained unchanged for 19 years.

The low differentiated carcinomas of the thyroid, especially those of the anaplastic type, are often radiosensitive but in such cases distant

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metastases are already usually present before treatment is commenced. In spite of the fact that the primary tumour often rapidly disappears under radiotherapy, the patient dies, in the majority of cases, of metastases within a year.

Merely the results in cases operated upon only and/or in those operated upon and post-operatively treated with radiotherapy, are often reported. Carcinoma of the thyroid is, however, inoperable in 70—80 per cent of cases (BERTELSEN et al., GRAHAM and MCWHIRTER, PORTMAN, STOCKS (quoted by WADE), WATSON and POOL). It is thus necessary to know the results of treatment in both the operable and inoperable cases in order to obtain a correct perception of the prognosis.

I have considered it of value to analyse the cases of thyroid carcinoma, treated at Radiumhemmet, on the basis of the present opinion and knowledge concerning this tumour. The main object has been 1) to ascertain the results of treatment in relation to the extent of the disease and to the histologic appearance of the tumour, 2) to determine the value of radiotherapy and especially teleradium, in the treatment of the disease, 3) to find out, if possible, the treatment of choice.

Material

The material consists of 144 consecutive cases of thyroid carcinoma, treated from 1935 to 1946. The surgical treatment has been carried out in different county hospitals and, in a small number of cases, at the Surgical Clinic of Karolinska Sjukhuset. All cases have been treated with irradiation at Radiumhemmet, either as supplementary therapy in operated cases or as the sole method of treatment in inoperable cases.

Histologic verification of the tumour is absent in 36 clinically definite cases (25 per cent) in the material. Biopsies were considered inadvisable in these cases because of the advanced stage of the disease and/or the poor general condition of the patient. Histologic verification of the tumour is absent to about the same extent in other representative material. Twenty per cent of the cases of BERTELSEN et al., 25 per cent of the cases of PORTMAN, and 33 per cent of the cases of GRAHAM and MCWHIRTER as well as of PEMBERTON, lacked confirmation.

Sex

In the whole material, there is a preponderance of women. PEMBERTON mentions 63 per cent of women, WATSON and POOL 70 per cent, WARD 75 per cent, and BERTELSEN et al., together with GRAHAM & MCWHIRTER, 78 per cent. CADE states that the mean incidence in large numbers of collected cases is 67 per cent. In the present material the incidence of women is 67 per cent.

Age

Most cases of carcinoma of the thyroid have been reported as occurring between the ages of 40 and 70. It has been found by BERTELSEN et al., PEMBERTON and WARD, as well as in the present material, that two-thirds of the cases are between 40 and 70 years of age. BERTELSEN et al., and WARD stated that just under twenty per cent of the cases were under 40 years of age. In the present material, fifteen per cent of the patients were under 40.

Cases have been described in rather young subjects and in children of only 3 or 4 years of age. In most of these cases, the tumour was a papillary adenocarcinoma. BEAHRS et al., mentions that 15 per cent of 174 patients with papillary adenocarcinoma were less than 20 years of age. DUFFY and FITZGERALD have reported twenty-eight cases in which the patients were 18 years or younger. PEMBERTON stated that 2.2 per cent of his patients were under 20 years of age. These figures are all from America. In the present material, there are only two patients less than 20 years old (both aged 19). The histories in some cases, however suggest onset of the disease in early childhood. More active surgery,

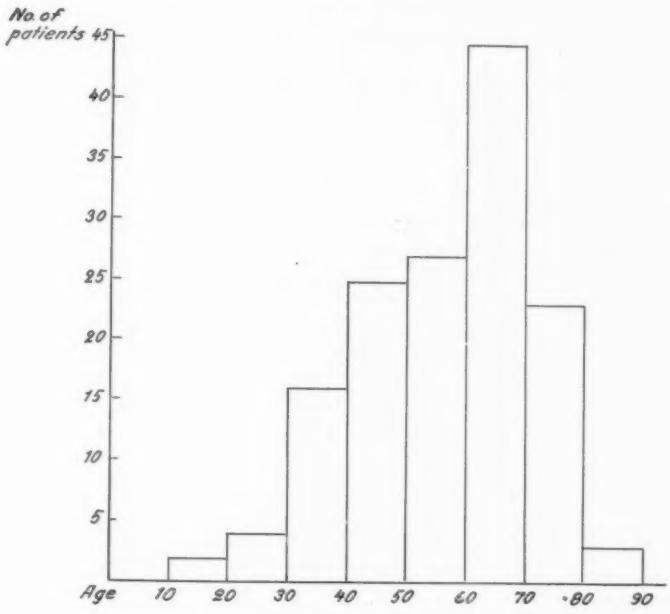

Diagram 1

as performed in America, in children with nodular goitre and/or "tuberculous glands" might perhaps reveal more cases of carcinoma of the thyroid in children in our country also. That this may indeed be so, has been substantiated by a case in recent years. A 13-year-old girl, with deposits of carcinoma of the thyroid in the glands on both sides of the neck, had been treated for "tuberculous glands" for many years before a biopsy was performed. By that time the tumour was already inoperable.

The age distribution in the present material is shown in Diagram 1. The youngest patient was 19 and the oldest, 88 years.

Stage of Disease

A fairly good appreciation of the composition of a material is obtained if an attempt be made to divide the cases into groups according to *the extent of disease at the time of treatment*. By such a grouping, one also finds out to how great an extent the cases were operable. I have divided the cases into four groups. The distribution has been determined by consideration of the clinical condition, operation findings and the result of histologic investigations.

Stage I: The primary tumour is mobile or only slightly fixed to the adjacent structures. No metastases.

Stage II: The primary tumour is mobile or only slightly fixed to the adjacent structures. Mobile lymph node metastases on one side of the neck.

Stage III: The primary tumour is extensively fixed to the adjacent structures. Cases with bilateral and/or fixed lymph node metastases in the neck.

Stage IV: Cases with distant metastases.

The number of cases in the various groups is shown in *Table I*.

Table I

Stage I	30 cases
Stage II	7 cases
Stage III	83 cases
Stage IV	24 cases

It is thus apparent that only a quarter of the cases were in the operable group, which is in good agreement with the conclusions of other authors (Bertelsen et al., Graham & McWhirter, Portman, Stocks [quoted by Wade] and Watson & Pool).

Diagnosis

Analysis of the present material substantiates the opinions of BERTELSEN et al., TROELL, WARD and others that an early clinical diagnosis of carcinoma of the thyroid is very rare. WARD goes so far as to state that if symptoms of cancer are present, the case is inoperable. Rapid growth, changed rate of growth, pain, fixation and hoarseness, as a rule, indicate an advanced stage of the disease. Early carcinoma of the thyroid gives not the slightest suggestion of being a malignant tumour.

Histology

There is wide variation in the histopathology of carcinoma of the thyroid. It is characteristic that the microscopic architecture, because of the varying grades of differentiation, is often very different in various parts of one and the same tumour. One also often notices markedly varying degrees of differentiation between the primary tumours and the metastases. Metastases may be both more lowly and more highly differentiated than the primary tumour. WARD has described a case in which the primary tumour consisted of a papillary adenocarcinoma. This was extirpated and the patient was symptom-free for many years but then died from metastases in the pleura and lungs. The secondaries in the lungs showed the same histologic structure as the primary tumour but the metastases in the pleura consisted of undifferentiated carcinoma.

DOBYNS and LENNON have shown rather beautifully how one and the same tumour may vary in degrees of differentiation. They transferred an undifferentiated human thyroid cancer to the anterior chamber of the eye of a guinea-pig. This tumour was further transplanted in nine generations over a period of three and a half years. The tumours were differentiated into various forms of carcinoma of the thyroid occurring in man, including adenocarcinoma and follicular adenocarcinoma with colloid formation. The differentiation often continued in the new generations but at times the progeny appeared to revert to a more primitive form. The tendency towards higher differentiation was, however, not constant throughout the whole tumour. Although there were more differentiated sections in the tumour, the other regions bore similar appearances to those of the primary tumour from the patient.

It is therefore easy to recognize how difficult it may be to classify certain thyroid carcinomas. There can be no definite borderline between the different groups. Many attempts at classification have been made, mostly based on a correlation of histologic structure with clinical course (HAAGENSEN; FRAZELL & FOOTE; WATSON & POOL — all in New York; WARREN; LAHEY & HARE — all in Boston; WARD in San Francisco,

PEMBERTON in the Mayo Clinic, Rochester, GRAHAM & MCWHIRTER in Edinburgh and BERTELSEN et al., in Copenhagen).

It was previously quite common to differentiate between carcinomas which arose in an adenoma from those tumours in which such an association could not be made (PORTMAN et alii). Many American authors now make a difference between adenomata with invasion and all other cases of carcinoma of the thyroid. This classification was introduced by WARREN (1941). More and more authors, however, have gone over to a simple classification which in the main follows the degree of differentiation within the tumour. There are usually three common groups, papillary adenocarcinoma, alveolar adenocarcinoma and small cell carcinoma. The latter two are then often each divided into two sub-groups.

In the present material from Radiumhemmet the cases have been grouped according to the histologic type predominant in the tumour. It was found possible to carry out such a grouping in 101 of the 108 cases, histologically verified. All slides have been reviewed by one experienced pathologist and I am indebted to Associate-Professor LARS SANTESSON for carrying out this work. Together we have classified the cases on a uniform basis. On going through the material, we have eliminated certain cases in which the original diagnosis of carcinoma was not confirmed. One of these cases which lived free from symptoms for many years after treatment, had been labelled by another pathologist as undifferentiated carcinoma but which proved on subsequent examination to have been a case of thyroiditis of the Hashimoto type. The cases have been divided into six groups. In certain cases, the tumours have been difficult to group, and have then been moved to the group with the highest degree of differentiation in accordance with the generally accepted practice in the classification of cancer.

Classification

Group I: Highly differentiated adenocarcinoma. The structure in this type is highly differentiated, not papillary. The cells are of similar appearance and without polymorphism. In several cases, one cannot decide merely from the appearance of the cells and the general structure of the tumour whether the condition is a malignant one but obtains definite evidence from the fact that the tumour has grown through the capsule and destroyed the surrounding normal thyroid tissue. This tumour is termed "orderly follicular carcinoma" in the literature. Those cases described as "benign metastasizing goitre" also belong to this group. It has been shown (FETZER, WARD et alii) by careful serial sectioning of the tumour in such cases that there are always one or two regions where the growth has penetrated the capsule and destroyed the

adjacent tissue. This work may prove, however, to be very time-consuming.

Group II: Well-differentiated papillary adenocarcinoma. This tumour is most characteristic and of a well-known and defined type. The tumour may be comparatively cystic or solid, depending to what degree the cystic spaces are filled with papilliferous tissue. It is as a rule very slow growing.

Group III: Moderately high differentiated adenocarcinoma. This tumour has well-developed acini and is termed alveolar adenocarcinoma in the literature. The acinous structure must be obvious throughout most of the sections. Regions of high differentiation may also appear in this type of tumour. This must, however, not dominate the structure.

Group IV: Low differentiated adenocarcinoma. In this tumour the cells are massed together in a compact fashion showing here and there a residual or obvious adenomatous structure, which may be difficult to find in the section. To this group belong those tumours which are termed "small cell carcinomas, compact type" in the literature.

Group V: Giant cell carcinoma. Wellknown, characteristic tumour with plenty of giant cells. This tumour is with regard to the grade of differentiation comparable with cases in group VI.

Group VI: Undifferentiated carcinoma (with sarcoma-like growth). This tumour is called "small cell carcinoma, diffuse type" in the literature. The differential diagnosis from a similarly growing sarcoma may present difficulties, which is also shown by the earliest name of carcino-sarcoma given to the tumour.

The division of the cases into the various groups is shown in *Table II*.

Table II

Classification

Group I	9 cases	(8 per cent)
Group II	15 cases	(14 per cent)
Group III	37 cases	(34 per cent)
Group IV	24 cases	(22 per cent)
Group V	3 cases	(3 per cent)
Group VI	13 cases	(12 per cent)
Unclassified	7 cases	(7 per cent)

In the unclassified cases, the histological material was not adequate for the purposes of classification.

Carcinoma of "Lateral Aberrant Thyroid"

LAHEY et al. (1951) have now abandoned the theory that the "aberrant thyroid", of which there has been much discussion, was truly an

aberrant thyroid. WILLIS has carefully studied this subject. He has found no evidence that developmentally aberrant thyroid tissue ever occurs in a lateral situation. KEITH (quoted by WILLIS), with a wide experience of developmental anomalies of the head and neck, has never seen or read of an unequivocal instance of the presence of a mass of detached normal thyroid lying laterally. WARREN and FELDMAN have studied a series of 57 cases of lateral "aberrant" thyroid tumours. There were only 8 cases in which a cancer of the thyroid was not found. Of these, the thyroid glands of 4 patients were not removed, having been regarded as negative at operation. In the remaining 4 cases the thyroid had been previously removed in another hospital and was not available for study. On physical examination the thyroid had been stated to be negative in 5 cases, yet at operation a tumour larger than 1 centimeter in diameter was found. A tumour less than 0.5 centimeter was discovered on microscopical examination in one case. According to CRILE a primary tumour in the thyroid gland is invariably found by the pathologist in cases of "aberrant" thyroid tumours. Lateral "aberrant" thyroid tumours should therefore be considered and treated as metastases from a primary carcinoma of the thyroid gland.

The primary tumour in such cases may be quiescent for many years. In the present material lymph node metastases on the left side of the neck were extirpated in one patient. The thyroid on physical examination was stated to be negative. Five years later the primary tumour was detected in the left thyroid lobe. It was, however, then inoperable but after irradiation the patient lived another three years. The tumour was classified as Group IV. (The primary tumour in this case commenced to grow after oophorectomy on both sides had been performed.)

Treatment

Opinion appears to be unanimous that operation should be performed if there is a reasonable prospect of removing all carcinomatous thyroid tissue. It seems also well established that a combination of surgical treatment and irradiation gives the patient a better chance than does operation as the sole method of treatment. WATSON & POOL state that this attitude is shared by the largest American clinics.

Operability of carcinoma of the thyroid depends on the stage of disease and to a certain extent on the histologic type of tumour. PEMBERTON has expressed the American attitude to operability. He states that "in the absence of distant metastasis, the relative fixation of the tumour is the most important feature to be considered in determining operability. Tumours which are completely fixed to all the contiguous structures should not be operated on, for it is obvious that the risk

involved in extirpating the tumour is out of proportion to the amount of benefit that one could hope to obtain. However, if the mobility is limited in such a way as to suggest that the carcinoma has perforated the capsule of the gland at one place only, then exploration is justifiable, for frequently in such instances the tumour can be removed in its entirety. This procedure is especially applicable in cases of extensive carcinoma of the papillary adenomatous type."

It goes without saying that if carcinoma is suspected, the operation should be extensive enough to remove all malignant tissue. Most surgeons, however, agree with WARD that at least one recurrent nerve, one parathyroid gland and both carotid arteries should be preserved. In America (CRILE, LAHEY, PEMBERTON, WARD), total hemithyroidectomy has been practised more often than subtotal thyroidectomy. The contrary state of affairs seems to have been the rule in Europe (BERTELSEN et al., GRAHAM & MCWHIRTER, DE QUERVAIN, TROELL).

Total thyroidectomy is rarely indicated (GRAHAM & MCWHIRTER, TROELL). LAHEY nowadays never performs total thyroidectomy. He considers that the possibility of a cure in a case with tumours in both lobes is so small that there is no justification for injuring both recurrent nerves with the inevitable consequences.

Mobile lymph node metastases on one side of the neck form no counter-indication for operation. Carcinoma of the thyroid, however, with exception of the papillary type, seldom involves the lymph nodes until it has penetrated the capsule of the gland and then is usually inoperable.

Intentional preoperative *irradiation* is rarely practised. An inoperable case of thyroid carcinoma may, however, by radiation treatment be rendered operable. Post-operative radiation therapy is recommended by most authors in all operated cases (GRAHAM & MCWHIRTER, HARE & SALZMAN, PATERSON, TROELL). The purpose of this treatment is to try to eliminate the tumour or retard the growth of cancerous tissue not detected or not removable at operation. That this treatment has a definite value is indicated by the fact that the survival rates are higher in a group of patients who were treated by operation and irradiation than in a group who were only operated upon. (HORN et al., PEMBERTON, PORTMAN).

Roentgen treatment has been widely used. It seems, however, that it has been difficult to obtain a sufficient tumour-dose with this treatment, without severly affecting the normal tissue and the patient's general condition. GRAHAM & MCWHIRTER have not given more than about 3,500 r as a tumour-dose in three weeks. In most cases of carcinoma of the thyroid such a small dose may retard the growth of the tumour but not eradicate it.

Reports on the use of *teleradium* are very rare. CADE, however, regards teleradium treatment to be the method of choice in the majority of cases. He has used an apparatus containing 4 gm with a radium—skin distance of 8 cm. Tumour doses of 6,500—7,000 r have been obtained in 5—6 weeks.

Radium implantation is seldom used nowadays (CADE) and PATERSON regards this form of treatment as counter-indicated in all cases of carcinoma of the thyroid.

Treatment with *radioactive iodine* has proved to be of definite value in a small number of cases. Skeletal and soft tissue metastases have been influenced and occasionally caused to disappear. Patients have been relieved of pain and brought back to useful work; prolonged survival periods have resulted (CRILE; SEIDLIN et al.; WARD, inter alios).

However, only about 5 per cent of all cases of thyroid carcinomas take up radioactive iodine in such amounts that treatment is possible. In only 1—2 per cent of all cases it is possible to obtain a satisfactory effect from the treatment.

Most tumours which take up radioactive iodine in therapeutic doses have an orderly follicular pattern (Group I in the classification of the present material). In a certain number of cases, one can make a tumour take up radioactive iodine or in other cases increase the uptake by "throwing out" the normal thyroid tissue by surgical or radiologic thyroidectomy.

Thyroid cancer metastases often show various degrees of differentiation in the same case and the differentiation often takes various forms in the same metastasis. For this reason the uptake of iodine is generally inconstant in the metastases as well as in the same metastasis, as is shown by autoradiograms. One must therefore usually concentrate upon gradually dealing with and eradicating the metastases by repeated treatment.

Valuable surveys on treatment with radioactive iodine have been given by, inter alios, HAHN as well as LOW-BEER.

LEMON et al., have pointed out the possibility of relieving, by means of testosterone, the pain caused by skeletal metastases from a carcinoma of the thyroid that will not take up radioactive iodine. Objectively a certain degree of recalcification in the region of the skeletal metastases was obtained in one case.

Treatment of the present material.

In the present material from Radiumhemmet, operation has been performed in operable cases. These cases have then been treated postoperatively with teleradium. In the majority of inoperable cases, tele-

radium treatment has been given. In the remaining cases roentgen treatment has been used.

Distant metastases have been treated with roentgen. In one case, treatment with radioactive iodine has been administered.

The surgical treatment of the cases in Stage I has been as follows:

Extirpation of the tumour	12 cases
Resection of the tumour lobe	4 cases
Lobectomy	4 cases
Subtotal thyroidectomy	8 cases
Total thyroidectomy	2 cases

In all twelve cases in which only extirpation of the tumour was performed, the preoperative diagnosis was adenoma. WATSON & POOL reported that in a series of 62 primary operable cases of thyroid carcinoma the surgeon had made an inaccurate pre-operative diagnosis of thyroid adenoma in eleven. PEMBERTON found that in 60 per cent of the surgical cases the presence of a malignant tumour was not suspected clinically but was discovered at operation or on histologic examination.

The surgical treatment of the cases in Stage II has been as follows:

Subtotal thyroidectomy + neck diss.	2 cases
Resection of tumour lobe + neck diss.	1 case
Extirpation of primary and one lymph node met. (carcinoma of the thyroglossus duct)	1 case
Total thyroidectomy + ext. of lymph node met. in one side of the neck (multiple tumours were found in both lobes)	1 case
Extirpation of lymph node met. (No primary palpated. Thyroid not exposed at op. Eight years survival)	1 case
Extirpation of lymph node met. (No primary palpated at op. Thyroid not exposed. Inoperable primary found in the thyroid five years later (same side as met.)	1 case

The last two cases illustrate the unreliability of physical examination of the thyroid. The thyroid ought to have been surgically exposed in both cases at the time of operation on the lymph node metastases. The teleradium treatment given post-operatively, probably retarded the growth of the primary or eradicated the tumour in the first case. The primary at the time of treatment may not have been more than a few millimeters in diameter (CRILE, WARD).

In the majority of the cases in Stages I and II the surgical treatment thus seems to have been rather conservative and it appears most likely that, at least in certain cases, not all the tumour tissue was removed. All cases have also been treated post-operatively with teleradium.

In spite of the advanced stage of disease a number of cases in Stages III and IV were operated upon but it was not possible to remove all the tumour tissue. By these procedures, however, we could obtain tumour tissue for microscopic examination and histological classification of the tumour.

Teleradium treatment has been given with a 3 or 5 gm bomb with a radium—skin distance of 6 cm. The treatment fields have been 5 centimeters in diameter. Depending upon the size and extent of the tumour, three or more treatment fields have been used. Treatment up to skin tolerance has been given in the majority of cases. This means a direct skin dose to each field of 4,000—5,500 r, the dose depending upon the number of fields used and the distance between the centres of the fields. Daily skin doses of about 1,000 r have been administered. One series of treatment has as a rule been given but in some advanced cases two or more series have been prescribed.

We have found that treatment by teleradium has definite advantages over ordinary roentgen in cases of carcinoma of the thyroid. The patient tolerates larger skin doses and less reaction in the trachea and oesophagus is obtained. This is obviously of great importance to those patients who often previously, by reason of the pressure of the tumour upon the throat, have found it difficult to eat or to breathe. The risk of necrosis of the cartilage of the trachea is also diminished by reason of the lesser absorption by the cartilage of the hard gamma-radiation, a part of which has an energy of more than 1.5 MeV. In this manner, we have been able to administer a tumour dose of more than 6,000 r over a period of 3—4 weeks in cases of advanced, widespread tumours without the patient's general condition being made worse. The radiation reaction which may be intense for several days up to a week, has caused little inconvenience to the patient.

(One Imc-hour is calculated to equal 8.3 r when teleradium doses are given.)

Treatment Results

When the results of treatment in carcinoma of the thyroid are discussed, survival rates and not cure rates should be used; we know that this tumour may recur or form metastases many years after treatment.

In the present material of 144 cases, the majority of which have been irradiated only and the remaining cases treated by operation and postoperative irradiation, *the five-year survival rate is 46 per cent.* (In the 108 cases with histologic verification of the tumour, the five-year survival rate is 52 per cent.)

In American materials, five-year survival rates up to 50—60 per cent are reported (Cole et al., Hare & Salzman, Horn et al., Pem-

BERTON). On the other hand, the five-year survival rates in European materials remain at 25—30 per cent (BERTELSEN et al., GRAHAM & MCWHIRTER, DE QUERVAIN).

The variation between the American and European results is caused to a great extent by the different composition of the materials. A larger proportion of advanced and prognostically unfavourable cases are included in the European than in the American series. In the majority of the latter, alveolar adenomas in which the only indication of malignancy has been a sign of blood-vessel invasion — "adenomas with invasion" — are included as carcinomata. It has, however, been found that a change which appears to be a blood-vessel invasion, can be due to an artefact whereby acini may seem to lodge within the lumen of vessels. These tumours have an extremely good prognosis. HARE & SALZMAN state that the growths are apparently curable by simple surgical excision and should not be included as clinical cancer cases. Further, many of the American materials contain a notably high percentage of the prognostically favourable papillary adenocarcinomata (BEAHRS et al., 61 per cent, FRAZELL & FOOTE 46 per cent, LAHEY & HARE 46 per cent). In the material of Radiumhemmet, similar papillary adenocarcinomata appear in only 14 per cent of cases and in that of GRAHAM & MCWHIRTER, in 16 per cent.

One is not able, therefore, in general to compare directly the survival rates in different materials. The comparison becomes more accurate if carried out between different stages and histologic groups within the material.

Results in relation to stage of the disease

The prognosis for carcinoma in other organs is very much dependent upon the extent of the disease at the time of treatment. The same condition should obtain for carcinoma of the thyroid. In *Table III*, the five-year survival rates have been calculated for the different stages.

Table III

Results in relation to stage of disease

Stage I	(30 cases)	28 five-year survivals.
Stage II	(7 cases)	7 five-year survivals.
Stage III	(83 cases)	29 five-year survivals.
Stage IV	(24 cases)	3 five-year survivals.

We find that *with combined treatment of operation and teleradium in operable cases (Stages I and II) we have obtained a five-year survival rate of about 95 per cent.*

It seems evident that irradiation has a definite value as supplementa

therapy in the operable cases. HORN et al., PEMBERTON, PORTMAN found that the survival rates were higher in the group of patients treated by thyroidectomy and irradiation than in the group treated by thyroidectomy only.

GRAHAM & MCWHIRTER found in a group of 29 cases, similar to those in our Stages I and II, a five-year survival rate of 73 per cent. PORTMAN in a group of "early" cases had obtained a five-year survival rate of 83 per cent. The majority of these cases had been treated with operation and roentgen. WARD reported in a group in which the carcinoma was first diagnosed on pathologic examination, a five-year survival rate of 80 per cent.

For cases in Stage III we have obtained a five-year survival rate of 35 per cent (inoperable cases).

PORTMAN found that, following operation only, in advanced cases (comparable with our Stage III), all patients died of cancer within five years. But in a similar group in which radiotherapy was also employed, a five-year survival rate of 29 per cent was obtained. GRAHAM & MCWHIRTER found in a group of 84 inoperable cases with no distant metastases (comparable with our Stage III) a five-year survival rate of 16 per cent. In only 39 of these cases, however, had the roentgen treatment been adequate and of this more limited series, 29 per cent were alive at the end of five years.

In spite of distant metastases present at the time of treatment, three cases of the 24 in Stage IV survived more than five years.

Results in relation to histologic type of tumour

All cases in the present material, with microscopic verification of the tumour, *i. e.* 108 cases, have, as already stated, been placed in histologic groups. The cases in each group have been divided according to stage and the results for stage and group have been calculated. The results are recorded in *Table IV*.

In *Group I*, highly differentiated adenocarcinoma, six out of nine patients have lived more than five years after treatment (about 65 per cent).

Only two patients, both five-year survivals, belong to Stages I and II. All the other cases were in an advanced inoperable stage. The reason for this is the difficulty in making a histologic diagnosis of the tumour. If the pathologist is unsuspecting and fails to examine carefully several sections of the tumour for perforation of the capsule of the tumour and destructive growth in the surrounding thyroid tissue, the diagnosis of benign struma may easily be made. How tricky the whole matter may be is shown by the case of a nineteen-year-old girl who twice previously

Table IV

Results in relation to histologic type of tumour

	Stage I	No. 5 year survivals	Stage II	No. 5 year survivals	Stage III	No. 5 year survivals	Stage IV	No. 5 year survivals
Group I. (Highly diff. adenocarc.)	1	1	1	1	5	2	2	2
Group II. (Papill. adenocarc.)	8	8	1	1	4	4	2	—
Group III. (Moderate high. diff. adenocarc.)	15	14	3	3	18	10	1	—
Group IV. (Low diff. adenocarc.)	5	4	2	2	17	1	—	—
Group V. (Giant cell carc.)	—	—	—	—	3	—	—	—
Group VI. (Undiff. carcinoma)	—	—	—	—	7	3	6	—
Unclassified	1	1	—	—	2	—	4	—

had been operated upon for "struma". At the first operation she was only 10 and at the time of the second, 12 years of age. Subsequent examination of the microscopic preparations from these operations showed that the whole time the condition was one of carcinoma. On admission to Radiumhemmet the patient had extensive fixed recurrences on both sides of the neck. After teleradium treatment, she lived a further 13 years, 10 of which with bone metastases. The tumour thus ran a course of at least 23 years! In five other cases there is a similar history of two previous operations for "struma". In one of these, the first operation was carried out when the patient was one year old. He was 19 years when he came to Radiumhemmet; he received intensive teleradium treatment and has then lived without signs of distant metastases for eight years.

In one case, the diagnosis was made after the microscopic examination of a solitary metastasis removed from the scapula by operation. This patient had been operated on for "struma" eleven years previously. The patient has remained alive with metastases for eight years. A similar case with a lone metastasis of the scapula has been described by HERTZ.

HORN et al., who have a similar group in their material, reported that 7 out of 13 patients lived more than five years after treatment (about 54 per cent).

In *Group II*, papillary adenocarcinoma, 13 out of 15 patients have lived more than five years after treatment (about 85 per cent). The prognosis for this type of carcinoma is the best of all types. Nine cases belonged to Stages I and II and all these have survived for five years. The same applies to 4 cases in Stage III. It was previously considered that this tumour formed metastases only in the lymph nodes in the

neck and not in the lungs or skeleton. By degrees it has become evident, however, that both lung and bone metastases may appear if the case is followed for a sufficiently long period. Such sequelae are, however, rare (CRILE). In the present material one patient had died from lung metastases and another from secondary deposits in bone. One patient who had been operated upon twice for "struma" before admission to Radiumhemmet and gave a history of goitre dating back to the age of five, developed lung metastases five years after teleradium treatment. That was two years ago and she is still alive and without symptoms.

For papillary adenocarcinoma, other authors report survival rates of 70—80 per cent (CHRISTENSEN & BERTELSEN, FRAZELL & FOOTE, HARE & SALZMAN). HORN et al. give a survival rate of 64 per cent and GRAHAM & MCWHIRTER place the survival rate at 40 per cent.

In *Group III*, moderately high differentiated adenocarcinoma, a *five-year survival rate of 73 per cent* was obtained. The prognosis for cases in Stages I and II appear to be excellent. Of 18 cases, all but one survived. The one exception died, without signs of a tumour, of a heart lesion two years later. If the case should prove to be in Stage III, the prognosis is worse, but still, 10 out of the 18 patients survived.

The five-year survival rate for similar cases reported in the literature is given as around 30 per cent (FRAZELL & FOOTE, HARE & SALZMAN).

In *Group IV*, low differentiated adenocarcinoma, a five-year survival rate of about 29 per cent was obtained. Of cases in Stages I and II, 6 out of 7 survived. The seventh patient died of lung metastases after two years. The prognosis is thus even very good for cases in Stages I and II. The cases in Stage III were very advanced ones. There were lymph node metastases in the neck in 10 cases on admission. Only one patient lived for more than five years. In the majority of cases, the course was extremely acute, with death intervening within a year.

FRAZELL & FOOTE, in a similar tumour group, obtained a five-year survival rate of 23 per cent and HARE & SALZMAN a five-year survival rate of 20 per cent.

In *Group V*, giant cell carcinoma, there were only three cases, all of which were in an advanced condition with enormous primary tumours and fixed lymph node metastases. All died within a year.

FRAZELL & FOOTE have no five-year survivals in similar cases. HARE & SALZMAN reported two five-year survivals out of nine cases.

In *Group VI*, undifferentiated carcinoma with diffuse growth, three out of thirteen cases lived more than five years (five-year survival rate of about 23 per cent). All the cases were very advanced on admission and lung metastases were present in six. In four other cases secondaries soon appeared in the lungs. In three cases there were soft tissue, generally

visceral metastases, present. In the majority of cases there were also extensive lymph node metastases in the neck. This type of tumour differs from the other types in that in no case in the group could skeletal metastases be found. All cases, except the five-year survivals, died within a year.

GRAHAM & MCWHIRTER recorded a five year survival rate of 14 per cent in forty-eight cases of undifferentiated carcinoma.

Radiosensitivity

Highly differentiated adenocarcinomas are as a rule not much affected by irradiation (FRAZELL & FOOTE, GRAHAM & MCWHIRTER, HORN et al.). It is our impression that in most cases it is possible to retard the growth of the tumour and in some cases to obtain a decrease in its size.

Some consider *papillary adenocarcinomas* to be radiosensitive (COLE et al., HARE) while others believe that in general, the tumours are resistant to irradiation (CRILE, GRAHAM & MCWHIRTER). The varying reports depend to a certain degree on the size of the dose of irradiation employed by the authors. In order to obtain some effect, one must usually give larger doses than those used by GRAHAM & MCWHIRTER (3,500 r to the tumour over about three weeks). Teleradium therapy was administered to one of our cases in three series of treatment extending over a period of eight months, a dose of 10,000 r being given direct to each of three skin fields. The patient was alive and free from signs of tumour fifteen years later. We agree with FRAZELL & FOOTE that in about a third of the cases, it is possible to obtain arrest of the disease for long periods of time and that cures may result.

Moderately differentiated adenocarcinomas are sensitive to irradiation to a varying degree. A number of cases are radiosensitive but in the majority of cases one has to be satisfied with the arrest of the disease for long periods. In one of our cases the patient died of "intercurrent disease" eleven years after treatment. In this case the tumour growth had been completely arrested and the patient suffered no inconvenience from the tumour.

Low differentiated adenocarcinomas are markedly radiosensitive in about half the cases. The remainder show but moderate radiosensitivity. GRAHAM & MCWHIRTER have had similar experiences.

Giant cell carcinoma is supposed to be radioresistant. The three cases in the present material were advanced ones and in very poor condition and it was only possible to give a few treatments. The tumour did not appear, however, to be radiosensitive.

Undifferentiated carcinomas are extremely radiosensitive. These tu-

mours, the course of which is very rapid, should be treated as urgent cases. They cause early compression of the trachea with resulting stridor and death. The effect of radiotherapy is dramatic. Within twenty-four hours the symptoms are alleviated and the tumour commences to diminish in size.

Results of treatment with radioactive iodine

One case in the present series has been treated with radioactive iodine. This was a highly differentiated adenocarcinoma with a good uptake in some of the skeletal metastases. Relief of pain was obtained but the objective effect was slight.

Is carcinoma of the thyroid a preventable disease?

Previous goitre exists in a large percentage of thyroid carcinomas. The average compiled from twenty different papers (CADE) on this subject is 71 per cent. In the present material 60 per cent of the patients have been aware of a goitre for more than one year. This goitre has, the whole time, either contained a slow-growing carcinoma or an adenomatous part which later has become malignant. It seems reasonable to assume that with a more active attitude to such goitres at an earlier stage, the total number of thyroid carcinomas should decrease, and the number of early cases increase.

The problem may also be discussed from another point of view. It has shown by large statistics that a certain percentage of clinically benign nodular goitres have, on microscopic examination, been disclosed as malignant. The gross incidence of carcinoma in cases of nodular goitre seems to be about 5 per cent (BEAHRS et al., 4.8 per cent, BERTELSEN et al., 5.8 per cent, CRILE 5.6 per cent, HORN et al., 6.3 per cent, and Ward 4.8 per cent). In cases of solitary nodular non-toxic goitre the chance of malignancy is still greater. The incidence of malignancy in such cases, according to COLE et al., as well as CRILE is about 24 per cent and according to CERISE et al., and to COPE et al., about 19 per cent. The possibility of a solitary adenoma being malignant is three times greater in a man than in a woman (COLE et al., COPE et al., and WARD).

WARD recorded an incidence of malignancy of 40 per cent in ten children under 15 years of age with nodular goitre.

It is now considered to be a wise rule to advise removal of all lumps discovered in the breast even though they may appear benign. It seems reasonable to practise the same rule when solitary nodules are detected in the thyroid.

Conclusions

The clinical diagnosis of an early carcinoma of the thyroid seems to be impossible, there being no special signs of malignancy at that stage. It is therefore impossible for an examiner, from physical signs only, to inform a patient that a nodularity in the thyroid is not malignant. He should rather advise operation. Many carcinomas of the thyroid are diagnosed only on microscopic examination.

Carcinoma of the thyroid in children seems to be more common than was supposed earlier. There are many patients in the present series who gave a history of goitre or enlarged nodes in the neck since childhood. In American materials about two per cent of the patients with cancer of the thyroid are under twenty years of age. In the present material there were two such cases. Carcinoma of the thyroid therefore should be suspected in children with nodular goitre and/or longstanding, enlarged nodes in the neck.

Lateral "aberrant" thyroid tumours should now be considered and dealt with as metastases from a primary carcinoma of the thyroid gland.

Operable cases of carcinoma of the thyroid should be treated by surgical removal of all cancer tissue. The other lobe should be exposed and examined, as multiple tumours in the thyroid are not uncommon. The operations performed in the present material have been rather conservative. In twelve cases, only extirpation of the tumour was carried out, the preoperative diagnosis being adenoma. Total thyroidectomy is rarely indicated. Mobile lymph node metastases in the neck constitute no counter-indication for operation.

If histologic examination of a lymph node metastasis in the neck admits the possibility of a carcinoma of the thyroid, the latter should be surgically exposed even if no tumour has been found on physical examination. In one such case in the present material no tumour was found on examination at the time of treatment and the thyroid was not surgically exposed. The primary in the thyroid was only detected five years later and was then inoperable.

In all operable cases post-operative teleradium treatment should be administered.

In seventy-five per cent of the cases in the present material the tumour was inoperable.

In inoperable cases, teleradium is the treatment of choice. Teleradium treatment is as a rule better tolerated by the patient than roentgen therapy. It is possible to obtain, in most cases, higher tumour doses with teleradium than with roentgen. With teleradium, tumour doses of about 6,000 r spread over three to four weeks can be administered in

advanced cases whereas when employing roentgen in similar cases, one has to be satisfied with a tumour dose of about 4,000—5,000 r.

The use of radioactive iodine in the treatment of carcinoma of the thyroid seems to be rather limited. One case in the present series has been so treated, with satisfactory result.

The results of treatment in carcinoma of the thyroid are very much dependent upon the stage of disease at the time of its initiation and the histologic type of tumour. As different materials vary in this respect it is of no value and can be misleading to compare the over-all survival rates.

In operable cases a five-year survival rate of 95 per cent was obtained.

In inoperable cases, without distant metastases on admission, the five-year survival rate was 35 per cent.

In operable cases the results seem to be somewhat independent of the histologic type of the tumour. No case of the giant cell or the undifferentiated carcinoma type was, however, operable.

In inoperable cases, without distant metastases on admission, the results of treatment were good in papillary adenocarcinomas, less good in highly differentiated adenocarcinomas (orderly follicular adenocarcinoma) and unsatisfactory in low-differentiated adenocarcinomas and undifferentiated carcinomas. Low-differentiated adenocarcinomas and undifferentiated carcinomas were, however, as a rule extremely malignant and had in the majority of cases formed metastases on admission.

In inoperable moderately high-differentiated adenocarcinomas, the results were surprisingly good. It seems evident that this was accounted for by the intense teleradium treatment given in the majority of cases.

In most cases of highly differentiated adenocarcinomas it was possible by radiotherapy to retard the growth of the tumour and in some cases to obtain a decrease in its size. The papillary and the moderately high differentiated adenocarcinomas were as a rule fairly radiosensitive. Some cases reacted very well to radiotherapy. Low-differentiated adenocarcinomas were markedly radiosensitive in about half the number of cases. Due to the advanced stage and the patient's poor general condition it was impossible in many of these cases, as well as in those of giant cell carcinomas, to carry out irradiation properly. Undifferentiated carcinomas were extremely radiosensitive but at the same time highly malignant, distant metastases appearing soon after treatment.

It seems that carcinoma of the thyroid, at least to some extent, is a preventable disease. It is generally agreed that it is good cancer-prophylaxis to remove nodular goitre surgically. By this means, carcinomatous degeneration in some adenomas is prevented, and certain

cases of early malignancy will also be detected. In 60 per cent of the cases in the present material the patient had been aware of a goitre for more than one year.

SUMMARY

An analysis of 144 cases of carcinoma of the thyroid, treated from 1935 to 1946. In operable cases, with combined treatment by operation and teleradium, a five-year survival rate of 95 per cent was obtained. In inoperable advanced cases treated with radiation, the five-year survival rate was 35 per cent. The treatment of choice in operable cases is surgical removal of the growth and post-operative treatment with teleradium. Inoperable cases should be treated with teleradium. The prevention of carcinoma of the thyroid and its detection at an early stage is best accomplished by removing all nodular goitres. In the present material sixty per cent of the patients had noticed a goitre for more than one year.

ZUSAMMENFASSUNG

144 Fälle mit Karzinoma thyreoideae, die während der Jahre 1935—1946 behandelt worden sind, werden analysiert. In operablen Fällen wurde mit der kombinierten Behandlung, Operation und Teleradiumbestrahlung, in 95 % eine Überlebungsquote von 5 Jahren erzielt. In nicht operablen fortgeschrittenen Fällen, die radiologisch behandelt wurden, war diese 5-Jahresquote 35 %. In operablen Fällen ist chirurgische Entfernung der Geschwulst und postoperative Behandlung mit Teleradium die Methode der Wahl. Inoperable Fälle sollten mit Teleradium behandelt werden. Die Prophylaxe gegen das Thyreoideakarzinom sowie dessen Entdeckung in einem frühen Stadium geschieht am besten durch die Entfernung aller Kropfknoten. Im vorliegenden Material hatten 60 % der Patienten ihre Struma länger als 1 Jahr bemerkt.

RÉSUMÉ

Analyse de 144 cas de cancer de la thyroïde traités de 1935 à 1946. Dans les cas opérables, le traitement combiné chirurgical et télécuriethérapique a donné 95 % de survies de cinq ans. Dans les cas avancés inopérables traités par le radium, le taux de survies de cinq ans a été de 35 pour cent. Le traitement de choix dans les cas opérables est l'exérèse chirurgicale de la tumeur et la télécuriethérapie post-opératoire. Les cas inopérables doivent être traités par télécuriethérapie. L'exérèse de tous les goitres nodulaires est la meilleure prévention et la meilleure détection à un stade précoce du cancer de la thyroïde. Soixante pour cent des malades de cette série se savaient porteurs d'un goitre plus d'un an.

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AUS DER UNIVERSITÄTS-FRAUENKLINIK (DIREKTOR: PROF. DR. H. MARTIUS), GÖTTINGEN, DEUTSCHLAND

DIE BEDEUTUNG DER IONISATIONSDICHTE FÜR DEN BIOLOGISCHEN EFFEKT BEI ULTRAFRAKTIONIERTER BESTRAHLUNG

von

R. K. Kepp

Die Apparaturen zur Erzeugung ultraharter Röntgenstrahlung oder schneller Elektronen, wie Elektronenschleuder (Betatron), Synchrotron und Linearbeschleuniger, arbeiten aus technischen Gründen mit sogenanntem Impulsbetrieb, so dass bei ihnen die Strahlung in zahlreichen Strahlenstössen innerhalb einer Sekunde ausgesendet wird. Eine kontinuierliche, wenig dicht ionisierende Strahlung lässt sich nur mit dem van de Graaff-Generator innerhalb gewisser zeitlicher Grenzen erhalten. Die Untersuchungen über das biologische Dosisäquivalent zwischen überharten und ultraharten Röntgenstrahlen bzw. schnellen Elektronen und Röntgenstrahlung von 200 kV haben ergeben, dass bei Mehrtreffervorgängen die wenig dicht ionisierenden energiereichen Strahlungen bei gleicher physikalisch in Luft gemessener Dosis biologisch weniger wirksam sind (G. SCHUBERT und Mitarbeiter, WACHSMANN und Mitarbeiter, QUASTLER und Mitarbeiter, GÄRTNER, SCHINZ, FRITZ-NIGGLI). Bei diesen Untersuchungen wurde jedoch nicht berücksichtigt, dass sie sich auf den Vergleich der Wirkung einer *kontinuierlich* verabfolgten klassischen Röntgenstrahlung mit der Wirkung von wenig dicht ionisierenden, aber im Sinne einer Ultrafraktionierung *diskontinuierlichen* Strahlungen erstreckten. Es war naheliegend zu überprüfen, ob die Ultrafraktionierung bei verschieden dicht ionisierenden Strahlen imstande ist, den strahlenbiologischen Effekt in unterschiedlicher Weise zu beeinflussen. Die Untersuchungen, über die im folgenden berichtet wird, wurden gemeinsam mit meinen Mitarbeitern DIECKMANN, HOF-

Vorgetragen auf dem 7. Internationalen Kongress für Radiologie in Kopenhagen am 20. Juli 1953.

Bei der Red. am 6. VIII. 1953 eingegangen.

MANN, MÜLLER und OEHLERT, sowie mit den Doktoranden ADAM, BERGMANN, BINNEWIES, FOCKEN, FRIEDRICH, PREISS, RANK, SCHUPPE und WENZEL ausgeführt.

Die Klärung der Frage, wie weit bei den energiereichen Strahlungen die Tatsache, dass diese Strahlungen ultrafraktioniert sind, den biologischen Effekt gegenüber der kontinuierlichen Verabfolgung verändert, ist mit erheblichen Schwierigkeiten verbunden, da hierfür eine kontinuierliche, genügend energiereiche Strahlung mit ausreichender Dosisleistung erforderlich wäre, wie sie aus den zugänglichen künstlich radioaktiven Substanzen nicht erhalten werden kann. Bei dieser Sachlage wäre daran zu denken, auf den Vergleich der Wirkung zwischen kontinuierlicher und ultrafraktionierter energiereicher Strahlung überhaupt zu verzichten und die Wirkung der energiereichen Strahlung mit der einer klassischen Strahlung von etwa 200 kV bei gleichartigem Impulsbetrieb zu vergleichen, woraus sich das den tatsächlichen Verhältnissen entsprechende biologische Dosisäquivalent zwischen den beiden Strahlenarten ergeben würde. Auch dieses Vorgehen war bis jetzt für uns nicht ausführbar, da die uns zur Verfügung stehende Elektronenschleuder der Siemens-Reiniger-Werke A. G. sich auf eine der klassischen Röntgenstrahlung entsprechende Energie nicht herabregulieren lässt. Um trotzdem einen Anhaltspunkt zu gewinnen, ob die Ultrafraktionierung einer Strahlung in Abhängigkeit von der Ionisationsdichte für den biologischen Effekt eine Rolle spielt, haben wir *Modellversuche* ausgeführt, in denen wir die Wirkung der Strahlung aus wenig gefiltertem Radium mit der einer weichen Röntgenstrahlung von 0.1 mm Cu Halbwertschicht, jeweils bei kontinuierlicher Bestrahlung und bei Impulsbetrieb, verglichen. Um brauchbare Dosisleistungen zu erhalten, musste allerdings das Verhältnis zwischen Impulsdauer und nachfolgender Pause wesentlich geringer angesetzt werden, als es z. B. bei der 6 MeV-Elektronenschleuder der Siemens-Reiniger-Werke A. G. mit 1 : 200 bis 1 : 2,000 besteht. Die Ultrafraktionierung wurde mit Hilfe einer stroboskopischen Scheibe aus Messing mit einer Bleieinlage erzielt, wobei freilich bei der Radiumbestrahlung der Gammastrahlenanteil, der bei der verwendeten Filterung von 0.2 mm Monelmetall 12 % der Gesamtstrahlung ausmachte, der Ultrafraktionierung nicht mit unterworfen werden konnte. Die Übereinstimmung der Dosisleistung bei kontinuierlicher Bestrahlung mit der mittleren Dosisleistung bei ultrafraktionierter Bestrahlung wurde durch entsprechende Veränderung des Abstandes zwischen Strahlenquelle und Objekt erzielt. Die Dosismessung der Radiumstrahlung wurde mit einer für Röntgenstrahlenmessungen gebauten Ionisations-Kleinkammer vorgenommen, in deren Wand ein unbekannter Teil der Radium-Betastrahlung absorbiert wurde. Die tatsächlich verabfolgten Radiumdosen waren somit höher als die gemessenen, so dass diese Dosismessung

nicht für eine Ermittlung des biologischen Dosisäquivalents zwischen Röntgen- und Radiumstrahlung zu verwerten war. Die Gleichheit der mittleren Dosisleistung bei diskontinuierlich und kontinuierlich verabfolgter Bestrahlung wurde neben der Ionisationskammermessung auch durch Filmschwärzungsversuche sichergestellt. Wenn auch die mit dieser Versuchsanordnung erreichte Art der Ultrafraktionierung mit der Strahlung aus den Apparaturen zur Erzeugung energiereicher Strahlen nicht verglichen werden kann, so gestatten doch die Ergebnisse, die mit ihr erzielt wurden, Rückschlüsse darauf, ob bei Ultrafraktionierung der Bestrahlung Unterschiede der biologischen Wirkung in Abhängigkeit von der Ionisationsdichte der Strahlung in Rechnung zu setzen sind.

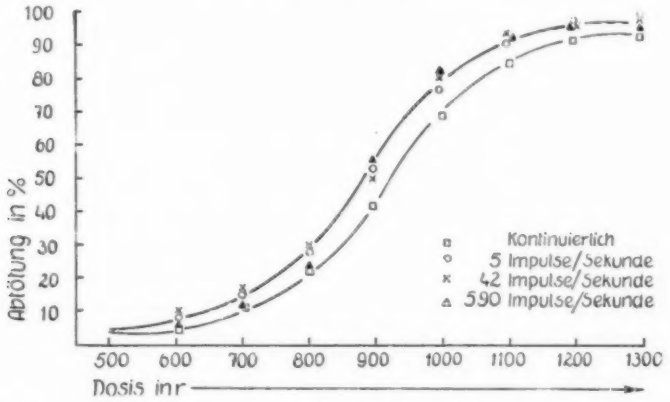

Abb. 1. Abtötungskurven bei Drosophilaeiern eines mittleren Alters von 4.5 Stunden nach kontinuierlicher und ultrafraktionierter Röntgenbestrahlung (HWS 0.1 mm Cu).

Bei Versuchen an *Drosophilaeiern* mit einem mittleren Alter von 4.5 Stunden nach der Eisammelperiode von 1 Stunde ergab sich bei einem Verhältnis von Impulsdauer zu nachfolgender Pause von 1: 2 und der Verwendung von 590, 42 und 5 Impulsen pro Sekunde folgendes: Bei *Röntgenbestrahlung* mit einer mittleren Dosisleistung von 27.4 r/min lag die Dosis-Effektkurve bei ultrafraktionierter Bestrahlung rund 10 % höher als bei kontinuierlicher Bestrahlung. Die Schädigungsraten bei ultrafraktionierter Bestrahlung verschiedener Impulszahl zeigten nur geringfügige Unterschiede innerhalb der biologischen Variationsbreite (Abb. 1). Die ultrafraktionierte Bestrahlung aus dem *Radiumpräparat* mit einer mittleren Dosisleistung von 21.2 r/min führte dagegen zu einem niedrigeren Effekt als die kontinuierliche Bestrahlung. Die Impulszahl machte sich dahingehend geltend, dass die Schädigungsrate mit

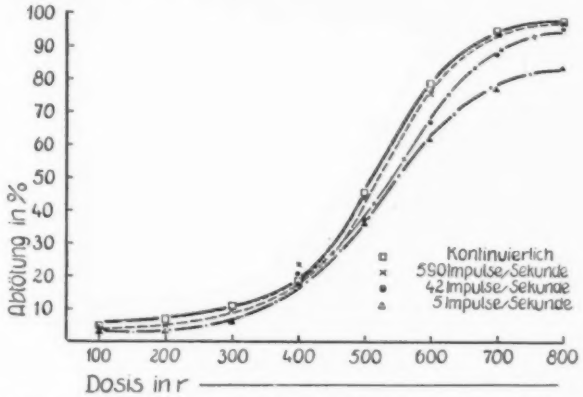

Abb. 2. Abtötungskurven bei Drosophilaeiern eines mittleren Alters von 4.5 Stunden nach kontinuierlicher und ultrafraktionierter Bestrahlung mit wenig gefiltertem Radium.

der Impulszahl anstieg (Abb. 2). Im Bereich der Halbwertdosis betrugen die maximalen Unterschiede zwischen den Abtötungsraten nach ultrafraktionierter und kontinuierlicher Bestrahlung 19.5 %. Jeder Kurvenpunkt wurde durch die Bestrahlung von 2,000 Eiern gesichert.

Versuche mit dem gleichen Verhältnis zwischen Impulsdauer und Bestrahlungspause und denselben Impulszahlen wie bei den Eiern von Drosophila melanogaster wurden an *Bacterium coli* ausgeführt. Die Ultrafraktionierung der *Röntgenbestrahlung* führte hier zu einer geringfügigen Verringerung der Abtötungsrate (Abb. 3). Nach ultrafraktionierter *Radiumbestrahlung* war die Schädigung bedeutend geringer als nach kontinuierlicher Bestrahlung. Im Gegensatz zu den Ergebnissen an Drosophilaeiern fiel die Abtötungsrate mit steigender Impulszahl ab (Abb. 3). Zu ähnlichen Ergebnissen gelangte auch W. HUBER, der bei Verabfolgung von energiereichen Elektronenblitzen eine höhere Inaktivierungsdosis für Bacterium coli fand als bei kontinuierlicher Elektronenbestrahlung. Diese Beobachtungen zeigen, dass unter bestimmten Einflüssen die Strahlenreaktion des Bacterium coli von der Art einer Eintrefferreaktion abweichen kann, wie es auch bei Veränderungen der Wachstumsbedingungen beobachtet wurde (ENGELHARD und HOUTERMANS).

Die Aufgabe weiterer Versuche war, eine Orientierung darüber herbeizuführen, wie weit bei einer wenig dicht ionisierenden Strahlung die *Veränderung* der *Impulszahl* und des *Verhältnisses zwischen Impuls- und Pausendauer* eine Änderung der biologischen Wirkung mit sich bringt. Für diese Versuche wurde die Strahlung aus dem wenig gefilterten

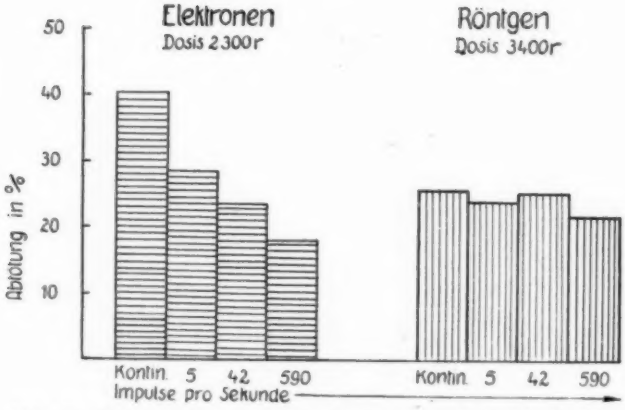

Abb. 3. Abtötungsrate von Bacterium coli nach kontinuierlicher und ultrafraktionierter Bestrahlung mit wenig gefiltertem Radium und Röntgenstrahlung (HWS 0.1 mm Cu).

Radiumpräparat verwendet. Die Impulszahlen pro Sekunde wurden zwischen 0.41 und 1,166, das Verhältnis zwischen Impuls- und Pausendauer zwischen 1 : 2.25 und 1 : 23 variiert. Mit der Veränderung des Verhältnisses zwischen Impuls- und Pausenlänge war zwangsläufig auch eine Veränderung der mittleren Dosisleistung verbunden. Diese bewegte sich zwischen 19 r/min und 41 r/min.

Bei Eiern von *Drosophila melanogaster* mit einem mittleren Eialter von 4.5 Stunden machte sich der Einfluss der Impulszahl, bei konstantem Impuls-Pausenverhältnis und somit auch konstanter Dosisleistung, dahin bemerkbar, dass bei einer bestimmten Zahl von Impulsen pro Sekunde ein ausgeprägter Maximaleffekt eintrat, der bei grösseren und kleineren Impulszahlen deutlich absank. Dieser Maximaleffekt war dosisunabhängig, d. h. er wurde über den gesamten Verlauf der Dosis-Effektkurve einheitlich beobachtet. Ein Beispiel für diesen Effekt zeigt Abb. 4, aus der ersichtlich ist, dass bei der Dosisleistung von 22 r/min und einem Impuls-Pausenverhältnis von 1 : 10.4 der Maximaleffekt bei 133.3 Impulsen pro Sekunde beobachtet wurde. Die verabfolgte Dosis betrug 800 r, was aber unwesentlich ist, da der beschriebene Effekt auch bei den anderen Dosen beobachtet wurde. Wurde das Verhältnis zwischen Impuls- und Pausendauer und damit die Dosisleistung modifiziert, so ergab sich, dass die maximale Schädigung mit einer Vergrösserung dieses Verhältnisses zunehmend in den Bereich höherer Impulszahlen rückte, und dass der Effekt bei gleicher Dosis mit Vergrösserung des Impuls-Pausenverhältnisses zunahm (Abb. 5).

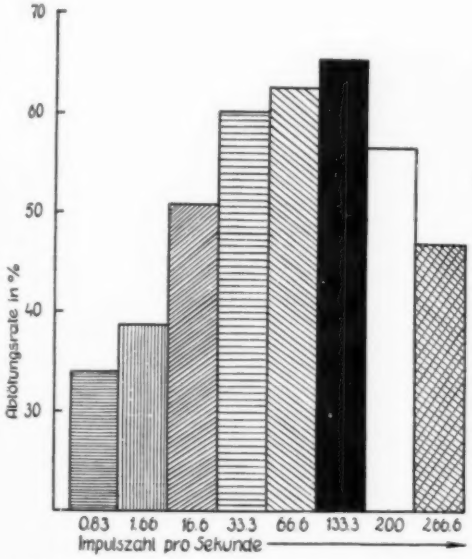

Abb. 4. Maximaleffekt der Abtötung 4.5 Stunden alter Drosophilaeier nach Bestrahlung mit wenig gefiltertem Radium bei 133.3 Impulsen pro Sekunde und dem Impuls-Pausenverhältnis von 1 : 10.4 (Dosis 800 r, Dosisleistung 22 r/min).

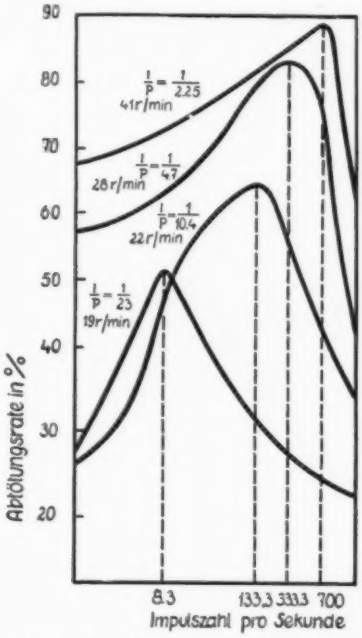

Abb. 5. Verschiebung des Maximaleffektes der Abtötung 4.5 Stunden alter Drosophilaeier nach Bestrahlung mit wenig gefiltertem Radium in den Bereich höherer Impulszahlen und Steigerung des Effektes bei Vergrösserung des Impuls-Pausenverhältnisses (Dosis 800 r). Die Intervalle der einzelnen Kurven sind aus Vergleichgründen übereinander geschoben.

Die Mitosenzahl in den Wurzelspitzenzellen von *Hordeum vulgare* liess nach ultrafraktionierter Bestrahlung mit 400 r aus dem Radiumpräparat bei den gleichen Dosisleistungen, wie sie für die Bestrahlung der Drosophilaeier verwendet wurden, einen geringeren Effekt gegenüber der kontinuierlichen Bestrahlung erkennen. Es wurde bei allen Impuls-Pausenverhältnissen eine Abnahme der Strahlenwirkung mit zunehmender Impulszahl beobachtet. Ein Beispiel für die Dosisleistung von 22 r/min mit dem Impuls-Pausenverhältnis von 1 : 10.4 gibt die Abb. 6. Ein Einfluss des Verhältnisses zwischen Impuls- und Pausendauer auf den Bestrahlungseffekt war nicht festzustellen. Diese Ergebnisse beruhen auf der Auswertung von insgesamt 1,600,000 Zellen.

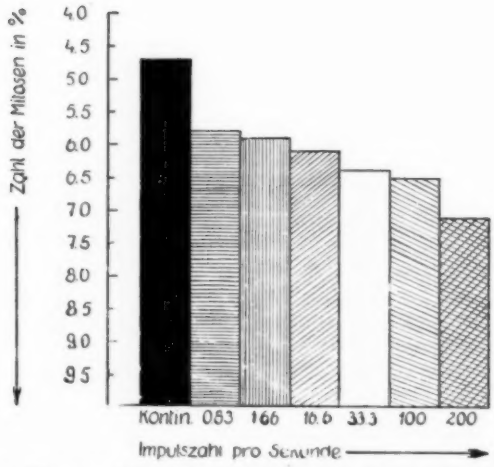

Abb. 6. Mitosenzahl in den Wurzelspitzenzellen von Hordeum vulgare nach kontinuierlicher und ultrafraktionierter Bestrahlung mit wenig gefiltertem Radium. Um das Absinken des Effektes mit zunehmender Impulszahl zu kennzeichnen, ist auf der Ordinate die Mitosenzahl im Sinne der negativen Ordinatenzählung aufgetragen. (Dosis 400 r, Dosisleistung 22 r/min, Impuls-Pausenverhältnis 1 : 10.4).

Die dargelegten Versuchsergebnisse gestatten, sowohl was die Dauer der Bestrahlungsimpulse, als auch was die Pausendauer zwischen den Impulsen betrifft, keinen Rückschluss darauf, wie sich bei den Apparaturen zur Erzeugung energiereicher Strahlungen die Ultrafraktionierung auf den biologischen Effekt auswirkt. Es liegen mit ihnen zunächst Einzelbeobachtungen auf einem bis jetzt kaum bearbeiteten Gebiet vor. Auf Grund unserer Versuchsergebnisse lässt sich jedoch sagen, dass auch bei der Ultrafraktionierung die Beeinflussung des biologischen Effektes durch die Ionisationsdichte mit in Betracht gezogen zu werden verdient. Die Zahl der Impulse pro Sekunde, aber auch das Verhältnis zwischen Impuls- und Pausendauer vermögen bei energiereicher Strahlung das Ausmass der biologischen Wirkung zu verändern, wenn auch die diesbezüglichen Untersuchungen noch keine einheitlichen Rückschlüsse zu ziehen erlauben. Es dürfte jedoch angezeigt sein, bei strahlenbiologischen Versuchen und bei der Strahlenbehandlung mit energiereichen Strahlen die Zahl der Strahlenimpulse pro Sekunde und das Verhältnis zwischen Strahlenimpuls und nachfolgender Pause zu berücksichtigen. Die komplizierten Zusammenhänge zwischen den verschiedenen Bedingungen der ultrafraktionierten Bestrahlung gestatten es nicht, an

dieser Stelle einen Erklärungsversuch für die beobachteten Einflüsse der Ultrafraktionierung auf den biologischen Effekt in Abhängigkeit von der Ionisationsdichte geben zu wollen.

ZUSAMMENFASSUNG

Strahlenbiologische Untersuchungen ergaben an Drosophilaeiern eines mittleren Alters von 4.5 Stunden und an Colibakterien eine unterschiedliche Auswirkung der Ultrafraktionierung auf den Bestrahlungseffekt bei Bestrahlung mit weicher Röntgenstrahlung und mit wenig gefiltertem Radium.

Die Veränderung der Zahl der Impulse pro Sekunde bei Bestrahlung mit wenig gefiltertem Radium führte an 4.5 Stunden alten Drosophilaeiern zu einem Maximaleffekt bei einer bestimmten Impulszahl, an Colibakterien und an den Mitosen in den Wurzelspitzenzellen von Hordeum vulgare zu einer Abnahme des Effektes mit zunehmender Impulszahl.

Die Veränderung des Verhältnisses zwischen Impuls- und Pausendauer bei Bestrahlung aus dem Radiumpräparat bewirkte an 4.5 Stunden alten Drosophilaeiern eine Verlagerung der maximalen Schädigung in den Bereich umso höherer Impulszahlen mit gleichzeitiger Steigerung des Effektes, je mehr dieses Verhältnis vergrössert wurde. An den Mitosen in den Wurzelspitzen von Hordeum vulgare liess sich eine Beeinflussung des Bestrahlungseffektes durch ein verändertes Impuls-Pausenverhältnis nicht feststellen.

Es wird die Bedeutung der Tatsache erörtert, dass es sich bei der Strahlung aus den Apparaturen zur Erzeugung ultraharter Röntgenstrahlung oder schneller Elektronen um eine ultrafraktionierte Strahlung handelt.

SUMMARY

Radiobiologic experiments in irradiating drosophila eggs of a medium age of $4^1/_2$ hours and bacterium coli by means of soft roentgen rays and of weakly filtered radium, showed a differential effect of the ultra-fractionation on the irradiation effect.

The change in the number of impulses per second by irradiation with weakly filtered radium, lead to a maximal effect in these eggs at a definite number of impulses. In bacterium coli and in the mitoses of the root tip cells of hordeum vulgare a decrease of the effect is produced by an increasing number of impulses.

In radium irradiation, the change of the proportion between duration of impulse and pause produced on $4^1/_2$ hours old drosophila eggs a shift of the maximal lethal effect into the region of the higher number of impulses; the effect being the greater the more the above proportion was increased. In the mitoses of the root tips of hordeum vulgare, however, a change of the radiation effect by means of a changed impulse-pause relation could not be observed.

The significance of the fact that when employing apparatus producing ultra-hard roentgen rays or fast electrons, we are dealing with an ultra-fractionated irradiation, is discussed.

RÉSUMÉ

Des expériences radiobiologiques consistant en l'irradiation d'œufs de drosophile âgés en moyenne de 4 heures et demie et de bacterium coli par des rayons roentgen mous et par du radium faiblement filtré ont montré un effet différentiel de l'ultra-fractionnement sur l'effet de l'irradiation.

La modification du nombre de coups par seconde par irradiation avec du radium faiblement filtré donne un effet maximum sur ces œufs pour un certain nombre de coups. Sur le bacterium coli et sur les mitoses des cellules de l'extrémité de la racine de hordeum vulgare, l'effet diminue quand le nombre de coups augmente.

Dans le cas de l'irradiation par le radium, la modification du rapport de la durée des coups et des arrêts a donné, pour les œufs de drosophile âgés de 4 heures et demie, une variation de l'effet léthal maximum qui est d'autant plus important que ce rapport est plus élevé. Cependant, la modification du rapport coups-arrêts n'a pas donné de modification observable des effets de l'irradiation sur les mitoses des cellules de l'extrémité de la racine de hordeum vulgare.

L'auteur examine l'importance du fait que quand nous employons un appareil produisant des rayons roentgen très durs ou des électrons rapides, nous avons affaire à une irradiation ultra-fractionnée.

SCHRIFTTUM

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SECONDARY ROENTGEN RADIATION FROM WAX, Al, Fe AND Pb AT TUBE VOLTAGES BETWEEN 40 AND 170 kV

by

Lars Lorentzon

The investigation now briefly described was carried out in 1947, using a roentgen therapy Metalix tube. The total filtration of the tube window was approximately 1 mm Al. A constant potential high-voltage generator with a Greinacher circuit was used. The experimental arrangement is shown in Fig. 1.

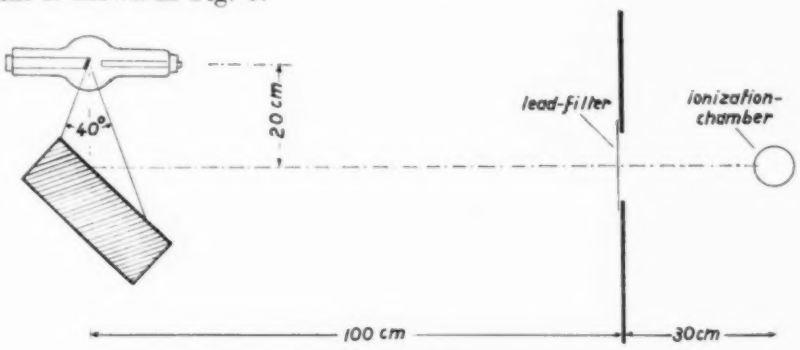

Fig. 1. The experimental arrangement.

The aperture angle of the primary beam of radiation amounted to 40°; at a focal distance of 1 metre this corresponds to a field-size of approximately 4,000 cm². Since it would have been difficult to use so large a phantom, a distance of 20 cm between the focus and the phantom was chosen. Apart from the air absorption, this has no influence on the measurements; the dose-rate of the primary radiation decreases with

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the square of the focal distance, but on the other hand, the irradiated surface increases with the square of this distance.

A shield with an aperture of 150 cm² was placed at 1 metre from the surface of the phantom; this aperture could be covered with lead filters of different thicknesses.

The ionization chamber, which has been described by THORAEUS (4), has walls of 0.8 mm bakelite and a volume of 560 cm³.

The following table shows the dose-rate of the primary radiation, measured in air, at a distance of 1 metre from the focus of the roentgen tube:

kV =	r/mA.min.
50	0.55
70	1.0
90	1.5
110	1.9
125	2.3
150	2.8
170	3.4

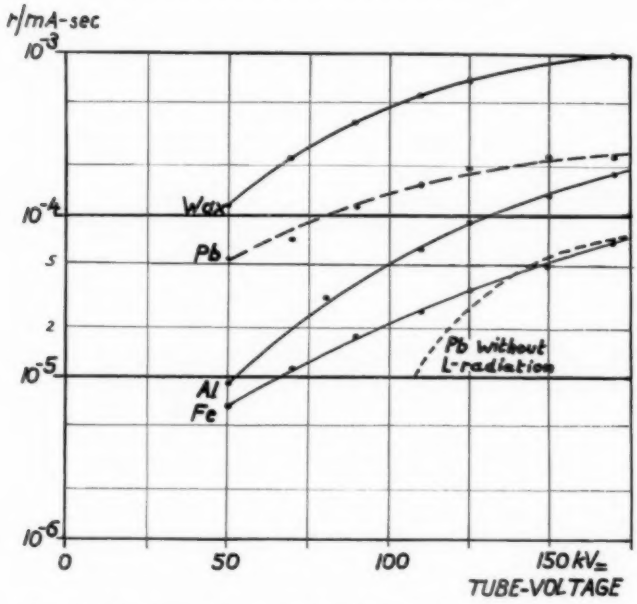

Fig. 2. The secondary radiation from Wax, Al, Fe and Pb at a distance of 1 m from the secondary source of radiation in r/mA.sec. as a function of the tube voltage.

Fig. 2 shows the dose-rate of the secondary radiation in r/mA.sec. at a distance of 1 metre from the phantom (the distance was actually 1.3 metre, but the values were recalculated for 1 metre). The highest value found was for wax. The fact that the dose-rate for the secondary radiation from lead is so high is due to its K and L radiation. The values recorded for iron may include a little part of its K radiation, despite absorption through the air and the wall of the chamber.

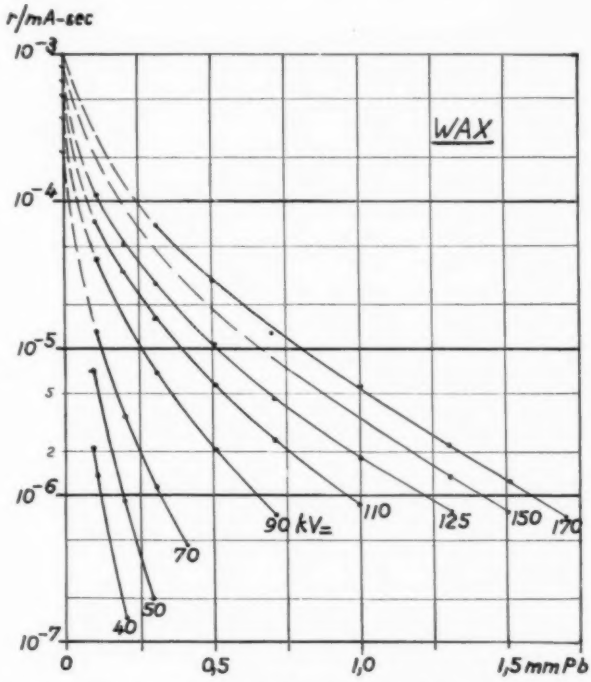

Fig. 3. The dose-rate for the secondary radiation from wax after filtration by lead in r/mA.sec. at a distance of 1 metre from the secondary source of radiation.

As already stated, the angle of the primary beam of radiation was 40° (the tube was not provided with any extra diaphragm). This corresponds to:

At 1	metre	distance,	a	field-size	of	approximately	4,000 cm²
» 0.7	»	»	»	»	»	»	2,000 cm²
» 0.5	»	»	»	»	»	»	1,000 cm²

If the aperture for the primary beam of radiation is reduced, the dose-rates shown in Figs. 2—6 must be recalculated in relationship to the field-size. The values for the secondary radiation given in Fig. 2 apply when the tube filtration is 1 mm Al. With other filtration, the dose-rate of the secondary radiation varies approximately with that of the primary radiation.

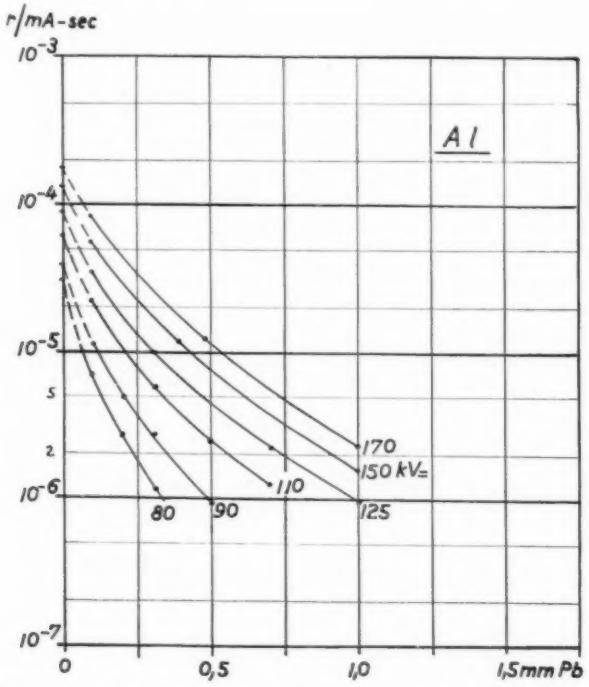

Fig. 4. The dose-rate for the secondary radiation from aluminium after filtration by lead in r/mA.sec. at a distance of 1 metre from the secondary source of radiation.

Figs. 3—5 show the dose-rate of the secondary radiation from wax, Al, and Fe as a function of the thickness of the lead filter in r/mA.sec. at a distance of 1 metre from the source of the secondary radiation. The broken parts of the curves were not measured; it is possible that their course might have been somewhat different.

The absorption curves for the secondary radiation from lead are shown in Fig. 6. These curves are of an entirely different nature from the corresponding curves for the secondary radiation from wax, Al and Fe (*cf.* Figs. 3—5).

The absorption curves for wax, lead and iron with a tube voltage of 170 kV= are assembled in Fig. 7. The broken curves "K" and "L" denote

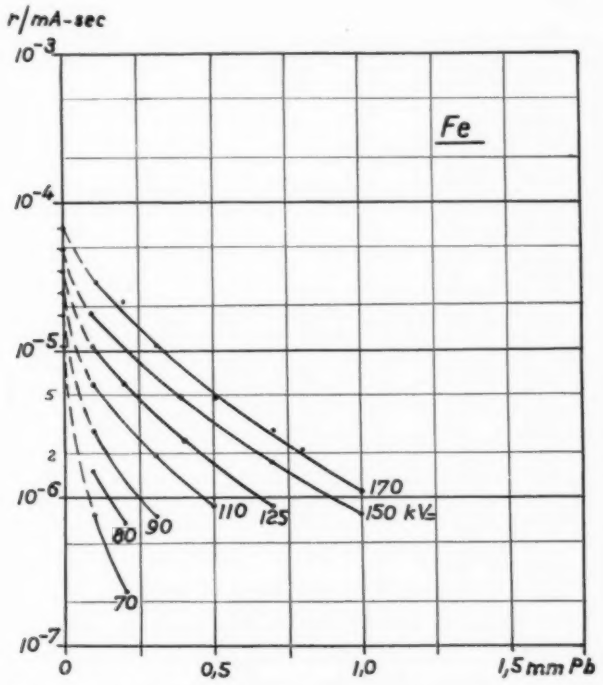

Fig. 5. The dose-rate for the secondary radiation from iron after filtration by lead in r/mA.sec. at a distance of 1 metre from the secondary source of radiation.

the calculated course of the absorption curves for the K radiation from lead (calculated with the mass absorption coefficient for 0.16 Å: $\mu/\varrho = 2.6$) and for the L radiation (calculated with the mass absorption coefficient for 1.0 Å: $\mu/\varrho = 75$).

Agreement between the calculated absorption curve for the K radiation and the measured absorption curve is good.

Since, from the point of view of radiation protection, the soft L radiation is usually of no consequence, those parts of the absorption curves for lead in Fig. 6 in which the L radiation was practically filtered off

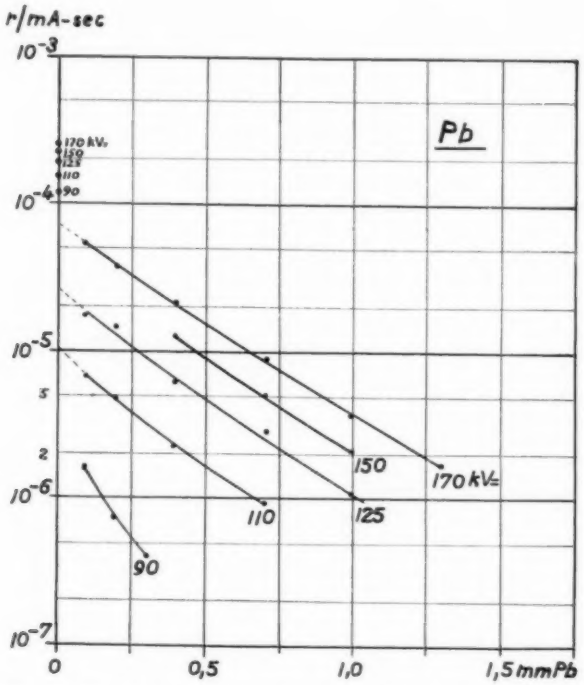

Fig. 6. The dose-rate for the secondary radiation from lead after filtration by lead in r/mA.sec. at a distance of 1 metre from the secondary source of radiation.

were extrapolated against a lead thickness of zero. The values thus obtained were used for the curve "Pb without L radiation" in Fig. 2.

The values for the secondary radiation from light substances such as tissue, water and wood are presumably similar to those for wax.

With respect to the spectral distribution of the secondary radiation, reference is made to papers by LINDELL (3) and WALSTAM (4) to be published in a following issue of this journal.

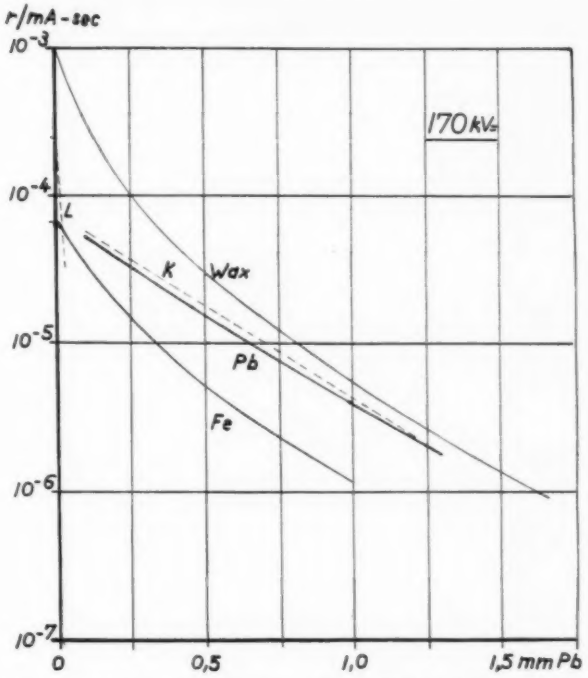

Fig. 7. Absorption of the secondary radiation from lead and the calculated absorption of the K and L radiation from lead at a tube voltage of 170 kV⎓.

SUMMARY

An investigation has been made of the secondary roentgen radiation from wax, Al, Fe and Pb at tube voltages between 40 and 170 kV, and of the absorption of the secondary radiation by lead. Curves have been assembled that may be used for radiation protection calculations in medical and technical work with roentgen rays.

ZUSAMMENFASSUNG

Sekundäre Röntgenstrahlung von Wachs, Aluminium, Eisen und Blei bei Röhrenspannungen von 40 bis 170 kV und die Absorption dieser Sekundärstrahlung durch Blei ist untersucht worden. Die Kurven sind so zusammengestellt, dass sie bei Strahlenschutzberechnungen für medizinische und technische Röntgenarbeit verwendet werden können.

RÉSUMÉ

L'auteur a fait des recherches sur le rayonnement secondaire émis par la cire, l'aluminium, le fer et le plomb sous des tensions allant de 40 à 170 kV et sur l'absorption du

rayonnement secondaire par le plomb. Il a tracé des courbes qui peuvent servir aux calculs de protection contre le rayonnement dans les utilisations médicales et techniques des rayons roentgen.

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